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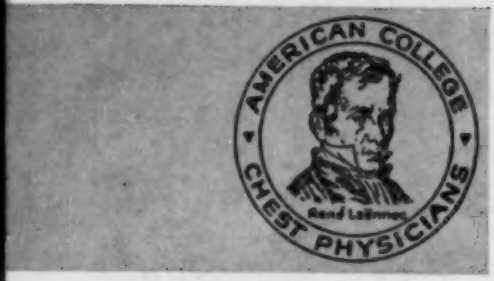
DISEASES of the CHEST



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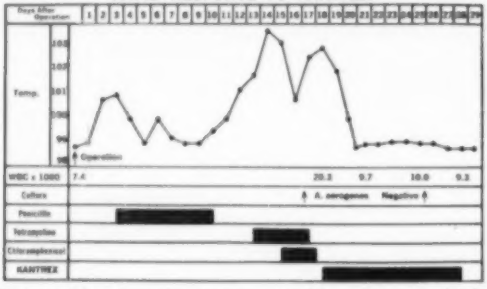

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DISEASES *of the* CHEST

OFFICIAL PUBLICATION

OF THE

AMERICAN COLLEGE OF CHEST PHYSICIANS

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112 East Chestnut Street, Chicago 11, Illinois, U.S.A.

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VOLUME XXXV APRIL, 1959 NUMBER 4

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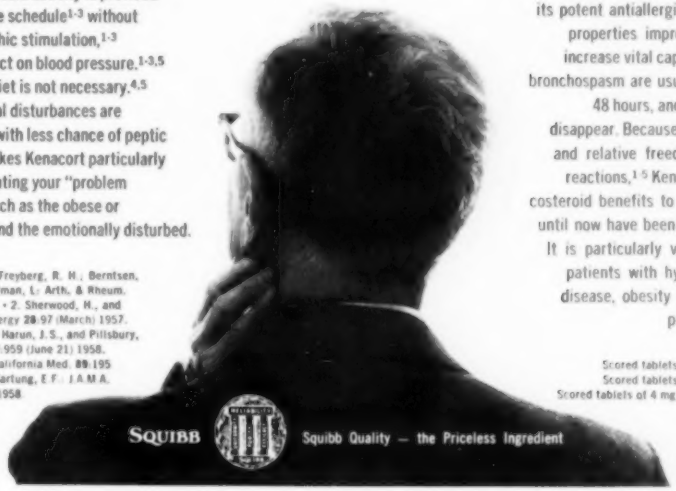
REFERENCES: • 1. Freyberg, R. H.; Berntsen, C. A., Jr., and Hellman, L.: Arth. & Rheum. 1:215 (June) 1958. • 2. Sherwood, H., and Cooke, R. A.: J. Allergy 28:97 (March) 1957. • 3. Shelley, W. B.; Harun, J. S., and Pillsbury, D. M.: J.A.M.A. 167:959 (June 21) 1958. • 4. Dubois, E.L.: California Med. 89:195 (Sept.) 1958. • 5. Hartung, E.F.: J.A.M.A. 167:973 (June 21) 1958.



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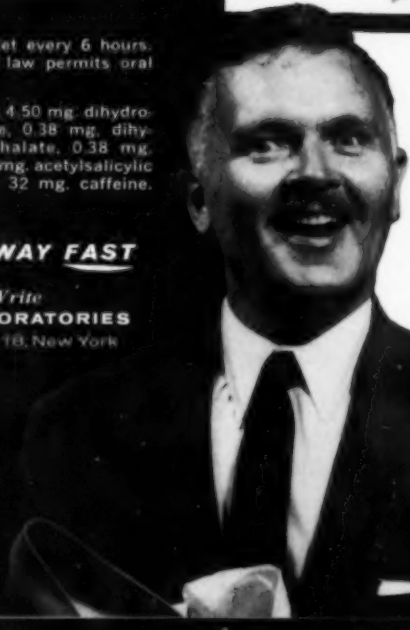

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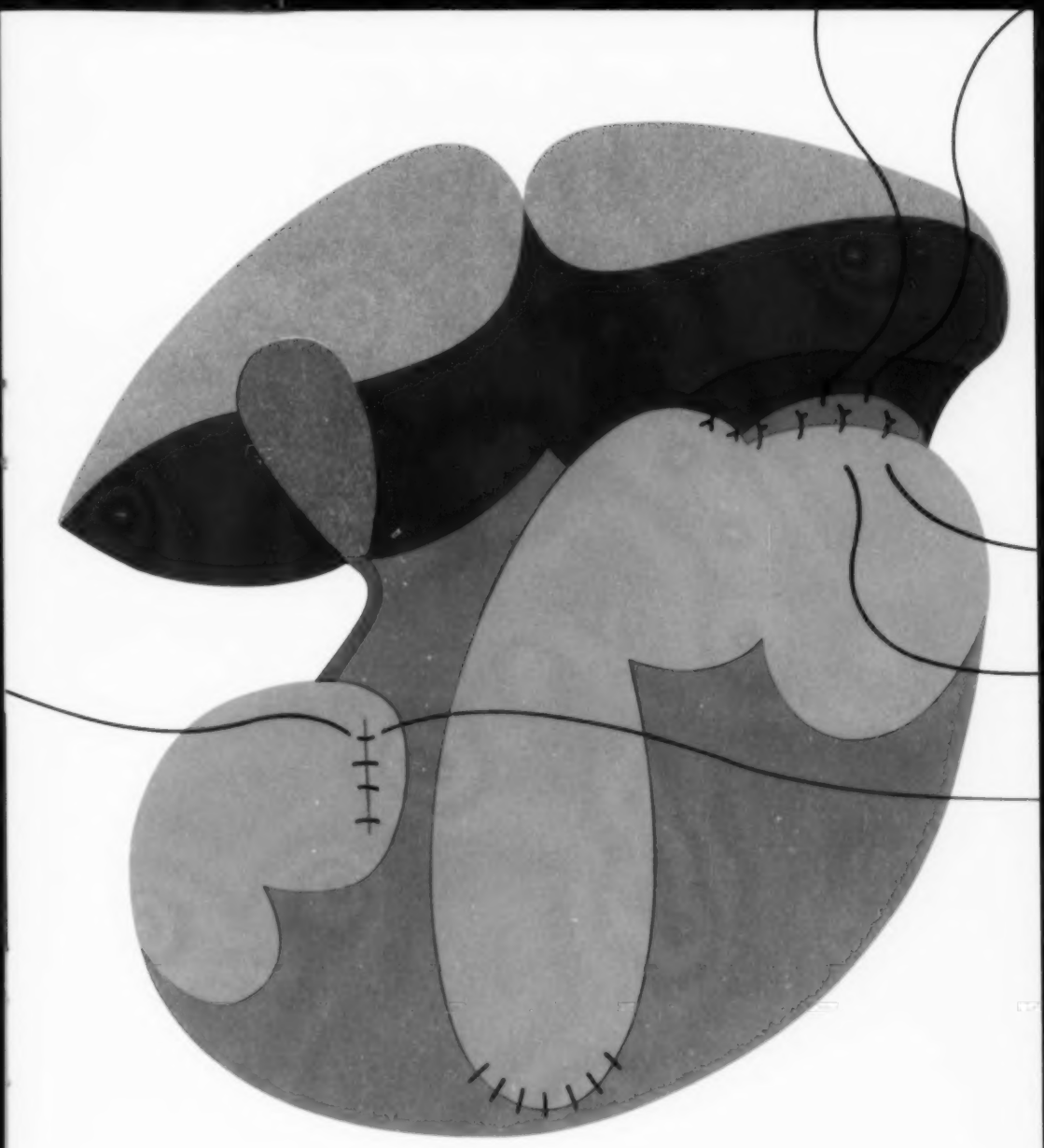

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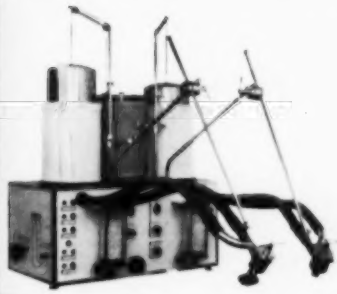

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Chapter Meetings

Tennessee Chapter, Memphis, April 13
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Texas Chapter, San Antonio, April 19
Oklahoma Chapter, Sequoyah State Park, April 19
Ohio Chapter, Columbus, April 22
New Jersey Chapter, Atlantic City, April 28
Arizona Chapter, Chandler, April 30
Florida Chapter, Bal Harbor, May 2
Kansas Chapter, Topeka, May 4
Wisconsin Chapter, Milwaukee, May 5
Mississippi Chapter, Biloxi, May 11
Illinois Chapter, Chicago, May 20

DISEASES of the CHEST

VOLUME XXXV APRIL, 1959 NUMBER 4

The Coexistence of Primary Lung Cancer and Other Primary Malignant Neoplasms*

CHARLES G. MOERTEL, M.D.,** HOWARD A. ANDERSEN, M.D., F.C.C.P.*** and ARCHIE H. BAGGENSTOSS, M.D.‡

Rochester, Minnesota

A solitary pulmonary lesion in a patient having a proved primary malignant neoplasm in another site presents a crucial problem in differential diagnosis. Many physicians feel that an heroic attempt to remove a pulmonary metastatic lesion by thoracic operation is an unjustifiably radical procedure. The possibility, however, that the presumedly metastatic lesion may in fact be a second and potentially curable primary malignant lesion must always weigh heavily in the thoughts of even the most conservative. Cotton,[1] as well as others, has presented differential factors in the diagnosis of primary and metastatic pulmonary neoplasms. He pointed out that a history of hemoptysis, the presence of cavitation, and a location in the upper part of the lung are all more characteristic of primary than of metastatic lung cancer. Whereas these features may help characterize a large series of patients, Kelly and Langstron[2] more recently have demonstrated that for the individual patient, the clinical differentiation between these two situations is difficult if not impossible.

The study by Kelly and Langstron[2] agreed with another by Cahan[3] in demonstrating that the presence of a second primary cancer in the lung is not an uncommon problem. In Cahan's series of 2502 cases of primary lung cancer seen at the Memorial Cancer Center, a total of 81 patients had proved primary cancers at some extrapulmonary site—a rate of occurrence of 3.2 per cent. During the same period at the same institution, only 18 patients were found to have a solitary pulmonary metastatic neoplasm. From a study of 22 patients undergoing exploratory operation for solitary pulmonary lesions diagnosed preoperatively as metastatic, Kelly and Langstron[2] reported that four were found at thoracotomy to have unsuspected primary lung cancers. They concluded that in patients in whom there is reasonable evidence that a primary malignancy has been

*Abridgment of portion of thesis submitted by Dr. Moertel to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Medicine.

**Fellow in Medicine, Mayo Foundation. The Mayo Foundation, Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.

***Section of Medicine, Mayo Clinic and Mayo Foundation.

‡Section of Pathologic Anatomy, Mayo Clinic and Mayo Foundation.

controlled, the presence of a discrete pulmonary lesion is an absolute indication for thoracotomy.

Selection of Cases

Cases for the present study were selected from those in which a histologic diagnosis of lung cancer was confirmed at the Mayo Clinic during the 10-year period from January 1, 1944, to December 31, 1953. The clinical and surgical findings were studied in all cases of this group that had been indexed under the diagnosis of a second malignant disease. Cases were accepted for study only if the diagnoses of both neoplasms had been confirmed by laboratory examination of surgical or necropsy specimens; a clinical diagnosis without a pathologist's confirmation was not considered sufficient evidence for inclusion in this study. Also, cases in which the lung cancer was diagnosed by cytologic examination of the sputum alone were excluded. Cases in which a neoplasm had been diagnosed and treated elsewhere prior to diagnosis of another neoplasm at the clinic were accepted for study only if the pathologic material from the former had been submitted to the clinic for examination. In brief, then, all the patients whose cases are included in our study had a lung cancer plus another unequivocally malignant neoplasm verified in the clinic laboratories during the period of this study.

The following criteria established by Warren and Gates[4] in 1932 have been generally accepted in the recent literature dealing with the problem of multiple primary malignant neoplasms, and are the criteria used for the selection of cases in the present study. 1. Each of the tumors must present a definite picture of malignancy. 2. Each must be distinct. 3. The probability that one is a metastatic product of the other must be excluded.

The fact that the lung is a common site for almost all types of metastatic malignant lesions compounds the difficulty of establishing a pul-

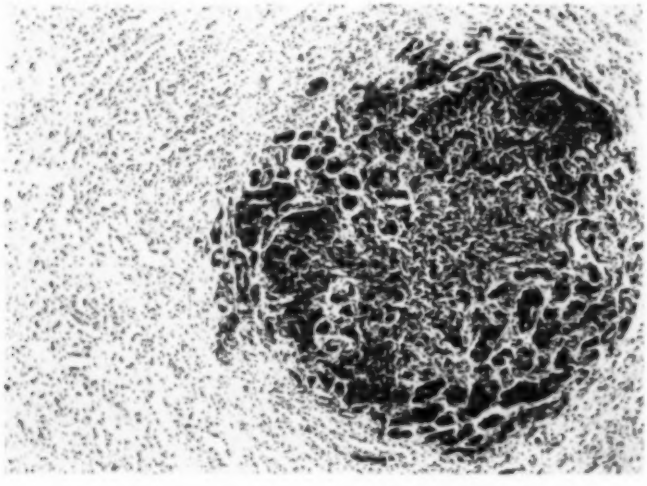

FIGURE 1: Bronchogenic carcinoma, small cell type, metastatic to adenocarcinoma, hypernephroma type of the kidney (hematoxylin and eosin; × 75).

monary lesion as a true second primary cancer. Several cases initially diagnosed as presenting second primary cancers in the lung were discarded from present study because after review of the pathologic material doubt existed as to whether the pulmonary lesion was actually a primary lesion. Some of these discarded cases possibly represented true but unconfirmable primary cancers.

Observations

During the 10-year period included in this study, a total of 1588 patients at the Mayo Clinic had the diagnosis of primary cancer of the lung, bronchus, or pleura confirmed by laboratory examination of specimens obtained at bronchoscopy, thoracotomy, or necropsy. Of this group a total of 65 patients, or 4.1 per cent, were found to have one or more other primary malignant neoplasms. Of these patients 59 were male and six were female.

In 27 cases the lesions were diagnosed simultaneously; in eight cases diagnosis of the pulmonary lesion preceded the diagnosis of the other neoplasm by periods of one to five years; and in 30 cases the diagnosis of the pulmonary lesion followed the diagnosis of the other neoplasm by periods of one to 29 years (average 9.6 years).

In 24 cases both lesions were diagnosed at operation only; in eight cases both lesions were diagnosed at necropsy only; and in 33 cases one or more lesions were diagnosed both at operation and at necropsy.

The distribution of the specific types of second primary cancers, shown in the table, does not seem significantly different from that to be expected in a random selection of patients of comparable age and sex with single malignant neoplasms. It is of interest that 37 of Cahan's series of 81 patients, or 46 per cent, were found to have their second primary lesions involving the oral cavity or larynx. He postulated that this association could represent the effect of a common etiologic agent in cancers of the oral cavity, larynx, and lung. In our study, only seven of 65 patients, or 11 per cent, had second primary lesions in these locations. Since the vast majority of patients with lung cancer are males in the older age groups,

TABLE I
SPECIFIC TYPES AND LOCATIONS OF ASSOCIATED PRIMARY MALIGNANT NEOPLASMS FOUND IN PATIENTS WITH PRIMARY LUNG CANCER

Types and locations	Cases	Types and locations	Cases
Carcinoma of		Carcinoma of	
Skin or lips	13	Pancreas and skin	1
Colon or rectum	9	Prostate and thyroid	1
Prostate	9	Leukemia or lymphoma	4
Bladder	5	Carcinoid (multiple) of ileum	2
Oral cavity	4	Fibrosarcoma	1
Breast	2	Malignant melanoma	1
Kidney	2	Seminoma	1
Larynx	2	Myeloma (multiple); epithelioma of skin	1
Ovary	1	Fibrosarcoma; epithelioma (multiple) of lips and skin; adenocarcinoma of parotid	1
Pancreas	1		
Stomach	1		
Thyroid	1		
Lip and prostate	1		
Mouth and skin	1		

this does not seem a disproportionate representation of cancers of the oral cavity and larynx.

Of incidental interest is the fact that at necropsy a primary carcinoma of the lung was found that had metastasized to a primary cancer of the kidney (figure). It appears that instances in which one malignant neoplasm is found to have metastasized to a second independent malignant neoplasm are exceedingly rare; when Ortega and associates[5] reviewed the literature in 1951 they could find only eight reported cases.

Comment

The evidence presented here as well as in the other works cited seems to establish definitely that the occurrence of an independent primary lung cancer in a patient with known malignant neoplastic disease at another site is not uncommon. Therefore no solitary pulmonary lesion in a patient with a previously diagnosed cancer may be simply assumed to be metastatic without positive laboratory confirmation. The present-day risk of thoracotomy in an otherwise doomed patient should be inconsequential when weighed against the possible tragedy of ignoring a potentially curable lung cancer on the grounds that it may be a solitary metastatic lesion. Indeed, even if the lesion should prove to be metastatic, hope may be found in Cahan's[3] records of many patients with surprisingly long survival and no evidence of metastasis to other sites following excision of a solitary metastatic pulmonary lesion.

SUMMARY

A total of 1588 cases of pathologically confirmed primary lung cancer were seen at the Mayo Clinic from January 1, 1944, to December 31, 1953. Of this group, 65 patients, or 4.1 per cent, were found to have an independent primary malignant neoplasm at some other site.

The distribution of the specific types of associated primary malignant neoplasms did not differ significantly from that expected in a comparable group of patients with single malignant neoplasms.

The coexistence of primary cancer of the lung and other primary malignant neoplasms occurs with sufficient frequency that no single pulmonary lesion may be assumed to be metastatic without positive pathologic confirmation. This series serves as further evidence supporting the conclusion of Kelly and Langstron[2] that in cases affording reasonable evidence that a primary malignancy elsewhere has been controlled, the presence of a discrete pulmonary lesion is an absolute indication for thoracotomy.

RESUMEN

Se han visto un total de 1,588 casos de cáncer primitivo del pulmón confirmados anatomopatológicamente en la Clínica Mayo, desde Enero 1, de 1944 hasta Diciembre 31 de 1953. De este grupo 65 enfermos o sea el 4.1 por ciento se encontró que tenian una neoplasia primaria maligna independiente en alguna otra parte del organismo.

La distribución de las formas especificas de la asociación primaria maligna no se difirió significativamente de lo que se esperaba en un grupo comparable de enfermos con neoplasias malignas únicas.

La coexistencia de cáncer primitivo del pulmón y de otras neoplasias malignas primitivas ocurre con suficiente frecuencia de tal modo que no se puede asegurar que haya una metástasis verdadera sin la confirmación histopatológica. Esta serie sirve para afirmar más la conclusión de Kelly y Langstron de que en casos que ofrezcan razonable evidencia de que un neoplasma primario en otra parte, ha sido dominado, la presencia de una lesión pulmonar discreta es una indicación absoluta para la toracotomía.

RESUME

Un total de 1,588 cas de cancer primitif du poumon confirmé anatomo-pathologiquement, ont examiné à la Clinique Mayo, de janvier 1944 au 31 décembre 1953. Sur cet ensemble 65 malades, c'est-à-dire 4,1% furent trouvés porteurs d'un cancer d'un cancer primitif indépendant siégeant à un autre endroit.

Les types spécifiques de cancers primitifs associés ne diffèrent pas d'une façon importante de ce qu'on a constaté communément chez un groupe comparable de malades atteints de néoplasie maligne à localisation unique.

La coexistence de cancer primitif du poumon et d'autres néoformations malignes primitives se rencontre avec une fréquence suffisante pour qu'on ne puisse jamais assurer sans confirmation anatomo-pathologique, qu'une lésion pulmonaire est métastatique. Cet ensemble d'observations apporte une démonstration ultérieure à l'affirmation de Kelly et Langstron que, lorsqu'on a la preuve incontestable qu'un cancer primitif a été traité efficacement quelque part, la présence d'une lésion pulmonaire discrète est une indication absolue de thoracotomie.

ZUSAMMENFASSUNG

Insgesamt 1588 Fälle von pathologisch-anatomisch bestätigten primären Lungenkrebsen durchliefen die Mayo-Klinik in der Zeit vom 1. I. 1944 bis 31. XII. 1953. In dieser Gruppe fanden sich 65 Patienten oder 4,1%, die einen davon unabhängigen primären bösartigen Tumor mit anderer Lokalisation aufwiesen.

Die Aufteilung der spezifischen Typen von gleichzeitig vorkommenden primären bösartigen Tumoren differierte nicht wesentlich von einer solchen, die zu erwarten war in einer vergleichbaren Gruppe von Kranken mit nur einem einzigen bösartigen Neoplasma.

Die Koexistenz von primärem Lungenkrebs und anderen primären bösartigen Neoplasmen ereignet sich mit genügender Häufigkeit, sodass man von einem einzelnen Lungenherd nicht mit Sicherheit sagen kann, er sei metastatisch ohne positive pathologisch-anatomische Bestätigung. Diese Serie dient als weiterer Beweis zur Stütze der Schlussfolgerung von Kelly and Langstrom,[2] wonach in Fällen, die genügend Anhaltspunkte dafür bieten, dass ein primärer bösartiger Tumor mit anderem Sitz beherrscht ist, das Vorliegen eines diskreten Lungenherdes eine absolute Indikation zur Thorakotomie bedeutet.

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Reversal of Tuberculin Reaction in Early Tuberculosis

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Introduction

The traditional concept that the tuberculin reaction when positive will remain so for the rest of the patient's life has been widely accepted for many years. The present study was carried out to detect tuberculosis in its earliest phases by means of a positive tuberculin reaction in individuals who reacted negatively to previous test or tests. These positive patients were then followed by repeated tuberculin tests for signs of change in their reactions. The opportunity to study the natural history of tuberculosis has been provided in the tuberculosis clinics of the Los Angeles Health Departments where hundreds of tests performed weekly on contacts made it possible to select individuals whose skin reactivity changed from a negative test to a positive one.

In the past two years 160 individuals have been discovered with a known negative test who have converted to a positive reaction within three months or within 12 months or were infants under one year of age who were found to have a positive reaction. It has been assumed in the case of infants under one year that they were early converters. One hundred twenty one individuals have been tested two or more times and 68 of these have changed from a positive reaction to a negative one. A total of 618 tests have been done on the entire group of 160 subjects. Although all of the subjects in order to be accepted in the study had an initial negative test or were under one year of age, the high rate of change from a positive to a negative test was very surprising.

A search of the literature has revealed a few papers in which the instability or reversability of the tuberculin reaction has been found. Dahlstrom[1] pointed to the finding of "calcified nodules, presumably of tuberculous origin" in individuals not reacting to tuberculin and raised the question as to whether or not this might indicate a loss of tuberculin allergy after complete healing. He showed a clear relation between the intensity of allergy and the probability of its ultimate disappearance. His data revealed that over 70 per cent of those showing the "weakest detectable reaction" (one plus) lost their allergy, and that 62 per cent of those individuals with a two plus reaction subsequently became negative. With respect to age factors, he further points out that reversability occurs in early life in an overwhelming majority and is rare in adult life.

Blatman, Rapmund, Newstrand, and Alexander[2] also state that "changes in tuberculin allergy have been surprising," and they found no difference in the patients with positive as opposed to negative gastric contents in

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regard to the degree of reduction of allergy to tuberculin. When they tested their 106 subjects, all under three years of age, 40 per cent were found to be negative at 12 months to the same dose of PPD or OT which was used initially. At 18 months, 54 per cent were negative, and when the negative subjects were retested with 1.0 milligram of OT, the overall percentage of negative skin tests became 40 per cent.

Galien and Hamman[3] reported in 1913 on patients who received repeat tuberculin tests and they showed a reversal to negative in 50 per cent of those retested. A recent report by Robinson, Meyer and Middlebrook[4] in 1955 indicated a reversal in skin allergy in a few patients treated with isoniazid (INH). In no instance have we found a study on reversal of tuberculin allergy in which the subjects were studied prior to the development of a positive skin reaction. A study of nurses by Tukey, et al.[5] revealed a lack of sensitization following repeated skin tests in subjects who had no allergy to tuberculin. However, they stated that "fluctuation was also expressed by frequent reversions to negative reaction." Aronson[6] reported on fluctuations in the tuberculin reaction among the BCG vaccinated Indian tribes which he studied and found the reversion rates to be highest at the Pima Agency, Arizona. Among the unvaccinated controls the fluctuation was higher than in other areas and "reversions from positive to 0.005 mg. of PPD to negative or doubtful were conspicuously high." It is of interest that a study of 80 individuals with disappearance of "skin hypersensitivity" was carried out by Paretzky[7] in the clinics of the Los Angeles County Health Department over 20 years ago. When retesting was done with a large dose (10 mg. of tuberculin) it was found that two-thirds of the subjects remained negative. The author concluded, "Immunity is considered as the causative factor of the disappearance of the specific skin hypersensitiveness."

Methods and Materials

Case Findings:

This study was carried out with the cooperation of the County and City of Los Angeles Health Departments and except for a few patients who were followed at the University of California Medical Center, and in sanatoriums, all subjects were registered either in the city or county tuberculosis clinics.

The selection of subjects was based on a known negative tuberculin test within a three month interval (Group B) or within a 12 month interval (Group C) prior to the finding of a positive reaction, except for infants (Group A) who were assumed to have had a previous negative test when the positive test was found under one year of age.

Tuberculin Testing:

The test material was purified protein derivative (PPD) administered intradermally on the ventral surface of the mid-forearm, and the doses employed were 5 units (.0001 mg.) of tuberculin in the city clinics and 25 units (.0005 mg.) of tuberculin in the county clinics. In nearly all instances the same dose was employed in the repeat tests in the respective clinics. The tests were applied by physicians who were highly experienced in the field of tuberculosis and were read by the same physicians or public

health nurses who were also experienced in this field. The readings were recorded in accordance with the standards established by the National Tuberculosis Association. The tests were read at 48 and 72 hours after injection and were graded according to the widest diameter of induration.

Negative — No induration
One Plus — 6-10 mm. induration
Two Plus — 11-20 mm. induration
Three Plus — > 20 mm. induration
Four Plus — Necrosis

The few doubtful tests were included in the negative readings. Repeat tests were carried out at three to six month intervals unless the physician in charge ordered otherwise.

Patient Care:

The diagnosis and management of the subjects remained the responsibility of the physicians in charge of the various clinics. In the county clinics, the subjects were divided into two groups on the basis of the family file number, the odd-numbered families were placed in the non-treatment groups, and the even-numbered families were placed in the treatment group. The treatment consisted of isoniazid, approximately 5 mg. per kilo per day administered in tablet form by mouth for a minimum of six months. A few were not treated at home but were sent to the sanatorium for care where they became patients of the sanatorium, and thus received varying treatment schedules in accordance with the physicians in charge. None of these latter patients are included among the reversion subjects.

Animal Studies:

Three groups of white guinea pigs were established, all weighing between 400—500 grams and in good health. They were all inoculated with 1.0 ml. of 0.1 mg. H37RV strain of *M. tuberculosis*. In group I, 23 animals were started on isoniazid (20 mg./animal/day) the day of inoculation. The drug was administered continuously in the drinking water and a dry feed was offered. Group II: 24 animals were started on the same dose of isoniazid 23 days following inoculation, and Group III: 24 animals received no medication. All of the animals were tested with old tuberculin, 0.1 ml. of a 1:20 dilution (5 per cent), intradermally, 21 days following the start of the experiment. Repeat skin tests were carried out at approximately three month intervals on five additional occasions between the start of the experiment on February 3, 1955 and the conclusion of the testing on May 13, 1956.

All of the remaining animals were autopsied at the conclusion of the experiment or at the time of death and gross findings in the spleen, liver, lungs, hepatic and tracheo-bronchial lymph nodes were evaluated and cultures were made of the spleen and lungs.

This report covers a two year period 1955-1957.

Results

At the present time there are 160 subjects under study who fit the criteria established. One hundred and twenty-one of these have been

TABLE I—RESULTS

Groups / Subjects	A Positive under 1 year of age	B Negative to positive within 3 months	C Negative to positive within 12 months	Total
Converters:	35	87	38	160
Retested Converters:	28	69	24	121
Reverters:	17 (60 per cent)	40 (58 per cent)	11 (46 per cent)	68

followed by repeated tests (517) and 68 or 56 per cent of these have shown a change in their skin reactivity from a positive reaction to a negative one. Three hundred and thirty-three tests were performed on these 68 reverting subjects for an average of approximately five tests per subject. In Group A, infants under one year of age, there are 28 retested subjects and 17 of these have shown a reversal of their positive reaction. In Group B, there are 69 retested subjects who were initially negative and converted to a positive reaction within three months of the negative test; 40 of these individuals have changed to a negative test. In Group C, there are 24 retested subjects who were initially negative who became positive within 12 months. Of these, there are 11 subjects who changed to a negative test. The above data is recorded in the accompanying Table I.

In Figure 1, the subjects from all three groups have been arranged according to the degree of skin reactivity. The total number of individuals expressed in percentages is recorded on the ordinate. The curve shows the percentage of subjects reverting at the various levels of reactivity and falls in nearly a straight line from 76 per cent (35/46) at

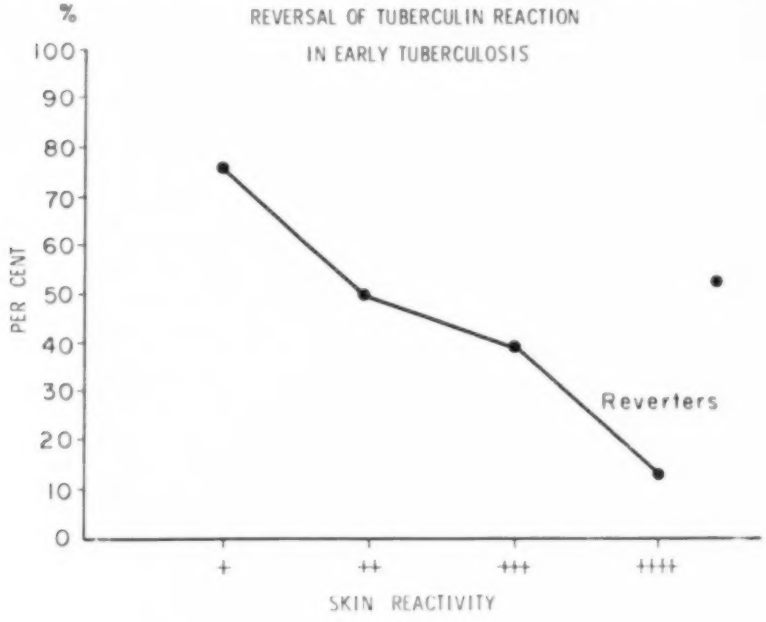

FIGURE 1

one plus, to 50 per cent (15/30) at two plus, to 38 per cent (9/24) at three plus, to 17 per cent (1/6) at four plus. There were 8 individuals out of 15 who changed reactivity in whom no degree of positivity was expressed. These are shown as a separate point at 53 per cent.

The age of the subjects has not been restricted and varied from infancy to old age. However, 84 per cent of the patients are under 16 years of age, and 50 per cent are under 6 years of age.

As the study progressed, the untreated group became about twice as large as a group receiving treatment in the home. 16 individuals were transferred from clinic and home care to sanatoriums. Among this group of patients, there are no data available on reversals. Many of these have not been retested as yet. We do not wish to attempt to evaluate the effect of therapy at this time because of the inequality in the retesting procedures. This is not the objective of this paper, but is cited only to point out that the majority of the subjects with changes in their skin tests were not in the treatment group.

The reversal rate was found to be higher in the subjects who were tested with the 25 unit dosage of tuberculin (PPD) than with the 5 unit test dose. The reversal rate in the County Clinic patients (25 units) was 64 per cent, and in the city clinics (5 units) the rate was 38 per cent.

Results of Chest X-rays:

A total of 97 individuals were examined roentgenologically. Of these 63 were found to have a normal x-ray film study. The reversal rate in these subjects was 48/63 or 76 per cent. Thirty-four individuals showed findings which were interpreted as "positive," with 20 of these read as "presumably inactive," and 14 as "presumably active." Ten of the 20 subjects with inactive findings showed a reversal of their skin test. None of the patients with "active" findings showed a reversal of their tuberculin reaction. These findings tend to correlate well with the rate of change in skin reactivity, the individuals with negative chest X-ray films showing a high rate of reversal as opposed to those with positive findings with no change in the skin tests found in patients with findings which were read as "presumably active."

Results of Animal Studies:

The results of the experimental tuberculosis in guinea pigs is summarized in Table II. There were three groups of animals, the first received treatment from the start of the experiment, the second after three weeks and the third group was untreated. The results of skin testing with OT is correlated with time in the various groups.

Cultures of spleens were all negative in Group I. There were no gross findings of tuberculous lesions in the first group. In Group II, three animals had a positive spleen culture and one of the three animals had a positive lung culture. All other cultures were negative. Two of the three animals showed gross findings in the spleen, one in the lung and two had enlarged lymph nodes as well with small lesions demonstrable grossly. Group III animals all showed severe signs of tuberculosis. These results are comparable to those reported by Peizer, Chaves and Widelock[8] in a much larger study. They showed no appreciable advantage in pre-treatment as opposed to treatment started simultaneously with infection,

but the immediate treatment method was found to be much more effective than when treatment was delayed for two weeks following inoculation.

The small animal study recorded here is presented to show a possible correlation of skin test reactivity with the severity of the infection. The treated animals never developed more than 1 to 2 plus reactions whereas the untreated animals developed plus 4 reactions uniformly.

DISCUSSION

The reversal of the tuberculin test is the primary reason for recording the data presented in this paper. It proved surprising in light of the traditionally held concepts regarding change in skin reactivity. Emphasis should be given to the fact that the subjects of this study were early converters with a known negative test unless the subject was an infant under one year of age. It has long been recognized that the majority of individuals who are infected by *M. tuberculosis* have little knowledge of when the primary illness occurred. It is possible that many primary infections are completely missed by our present methods of diagnosis of tuberculosis and because of the latent nature of the first infection. The use of the tuberculin test as a means of early diagnosis might be greatly increased if we were fully aware of its usefulness and reliability.

Dahlstrom[1] in 1940 was one of the first workers to study what he chose to call "the instability of the tuberculin reaction." He showed a clear relation between the intensity of allergy and the probability of its ultimate disappearance as we have shown in this present report. When one considers that the reversal rate is definitely correlated with the degree of the initial reactivity, it suggests that the change may not be expressed in terms of "instability" as logically as it might represent a degree of recovery on the part of the patient from a true but minimal infection. On the other hand, we must seriously challenge the concept that reactions between 6 and 10 mm. truly indicate infection by *M. tuberculosis*.

The British Research Council[2] recently analyzed a large group of adolescent children by comparing the various forms of tuberculosis in individuals reacting mildly (less than 15 mm. induration) to 3 tuberculin units as opposed to those reacting markedly to the same dose (greater than 15 mm. induration). The annual incidence of tuberculosis among the mild reactors was 0.78 per 1000 as compared to 2.93 per 1000 among the more marked reactors. In addition they reported a rate of 1.75 per 1000 of tuberculosis in those reacting positively to 3 T.U. as opposed to 0.74 per 1000 among those positive only to 100 T.U. and negative to 3 T.U.

Dahlstrom[1] points out the importance of age and the overwhelming majority of "unstable reactors" among children who showed a much higher reversal than adults concerning whom he states "reversion to negative proved rare in adults." Blatman, Rapmund, Newstrand, and Alexander[3] found a reversion rate of 54 per cent at 18 months in patients under three years of age. Their study was correlated with time and test dose rather than the degree of reactivity. When they used the largest commonly employed test dose of 1.0 mg. of OT, they found 40 per cent of the previously positive patients were negative. Although 50 per cent of the subjects in this study were under six years of age, no direct relationship of reversability to age could

TABLE II—RESULTS

Dates of Various Procedures	Group I	Group II	Group III
2/3/55	Inoc.	Inoc.	Inoc.
2/3/55	INH started		
2/24/55	Skin test	Skin test	Skin test
2/26/55	5+, 18—	24+, 0—	24+, 0—
2/26/55		INH started	
5/6/55	13+, 9—	23+, 0—	All strongly positive
9/2/55	4+, 14—	18+, 5—	Sacrificed
11/4/55	8+, 8—	19+, 0—	
2/9/56	9+, 7—	17+, 1—	
5/13/56	3+, 7—	17+, 0—	

be detected. The high rate may be related to age in part as 84 per cent of the subjects are children but the various groups are too small to permit critical analysis.

Early in the study, it became obvious that the value of repeating the skin test could not be overemphasized. We were continually surprised at the high incidence of negative tests in patients with previously positive reactions. The explanation is not clear but may represent fluctuations in sensitivity or healing of definite but slight infection with loss of reactivity. The low level and changing sensitivity after BCG vaccination would strongly suggest the latter mechanism. Whatever the answer to this question, it is apparent that a greatly increased understanding will be had by repeating the tuberculin skin test. Many families have been greatly relieved when repeat skin testing and x-ray film studies have failed to confirm a previous diagnosis. A further understanding of the full meaning of positive and negative tests is badly needed and particularly the significance of weakly positive reactions. Although the tuberculin reaction remains one of the best tests in clinical medicine today, the interpretation of the plus one and two reactions must be challenged and further study continued. On the other hand, repeated testing may well represent a means of detecting tuberculous infections early and learning more about the natural history of this disease. Dubos[10] stated, "in this country, at least, few are the communities where tuberculin testing at short intervals of time is organized to permit the recognition of tuberculous infection in its initial phase."

SUMMARY

A certain proportion of 160 subjects with a previous negative tuberculin test who became positive reverted to negative when followed by repeated tests in direct relationship to the degree of reactivity. Sixty eight subjects including those positive under one year of age showed a change from positive to negative in 76 per cent when their skin test was one plus, 50 per cent when two plus, 38 per cent when three plus, and only one individual with a four plus reaction showed a reversal. The reasons for this surprisingly high rate of change are unknown, but may represent early detection of tuberculous infection in individuals who might otherwise go unrecognized at this stage of their disease. By repeated testing of known negative and positive subjects, the natural history of the disease may become better understood. It is apparent that further study of the tuberculin test is needed before its significance can be fully appreciated.

Roentgenological studies revealed a direct relationship of findings with the degree of change in tuberculin reactivity, the patients with negative chest x-ray films showed a high rate of reversal; in contrast, no change in skin reactivity was found where the findings indicated a "presumably active" lesion.

When infected guinea pigs were treated with isoniazid, their skin reactivity was reduced when compared to untreated controls. It treatment was begun at the time of inoculation, some animals failed to develop any positive reaction and all had negative cultures. If treatment was delayed, all developed weakly positive skin test reactions and a few showed signs of tuberculosis at autopsy and by culture.

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RESUMEN

Cierta proporción de 160 individuos con previa reacción tuberculínica negativa y que se volvieron positivos, retornaron a la negatividad cuando se les siguió observando con repetidas pruebas, en relación directa con el grado de reactividad. Sesenta y ocho sujetos incluyendo niños que fueron positivos, menores de un años de edad, mostraron un cambio de positivo a negativo en 76 por ciento cuando su prueba cutánea era de una cruz, 50 por ciento cuando era de dos cruces, 38 por ciento cuando eran de tres cruces y sólo en uno de cuatro cruces se observó esa reversión. Se desconocen las causas de esta elevada proporción de cambios, pero puede representar una temprana detección de infección tuberculosa que de otro modo pasarían sin reconocerse en esta etapa de la enfermedad.

Por la repetida prueba de los negativos conocidos y positivos, la historia natural de la enfermedad puede comprenderse mejor. Aparentemente se necesita un estudio ulterior de la prueba tuberculínica para que su significación se conozca completamente.

Los estudios roentgenológicos revelaron una relación directa de hallazgos con el grado del cambio de la reactividad tuberculínica; los enfermos con películas negativas mostraron mayor frecuencia de reversión; por el contratio no se encontró cambio en

la reactividad cutánea cuando los hallazgos radiológicos indicaron una lesión "probablemente activa."

Cuando los cuyes infectados fueron tratados con isoniacida, su reactividad cutánea se vió reducida al compararse con los controles no tratados.

Si el tratamiento se empezó al tiempo de la inoculación algunos animales dejaron de presentar reacción positiva y todos tuvieron cultivos negativos. Si el tratamiento fué diferido, todos desarrollaron reacciones cutáneas débiles positivas y pocos mostraron signos de tuberculosis a la autopsia y por cultivo.

RESUME

Sur 160 individus ayant viré leurs réactions tuberculiniques, un certain nombre eurent de nouveau des réactions négatives après des examens répétés. Cette modification se produisit d'une façon tout à fait parallèle a l'importance qu'avaient eu les réactions. 66 sujets, comprenant des bébés ayant leurs réactions positives avant l'âge d'un an, eurent de nouveau des réactions négatives dans 76% des cas, quand leur réaction cutanée était légèrement positive (+) la négativation secondaire apparut dans 50% des cas quand elle était un peu plus positive (++) dans 38% lorsque la réaction était nettement positive (+++) et chez un seul individu porteur d'une réaction très positive (++++). Les raisons de ce taux considérablement élevé de retour à la négativité sont inconnues, mais cela être en rapport avec une détection précoce de l'infection tuberculeuse chez des individus qui autrement continueraient à être ignorés à ce stade de leur affection. En répétant les examens sur des sujets dont les réactions sont connues, on finit par mieux comprendre l'histoire de l'affection. Il semble que des études ultérieures sur le test tuberculinique soient nécessaires avant que sa valeur puisse être parfaitement appréciée.

Les examens radiologiques montrèrent une relation évidente avec l'importance du retour à la négativité des réactions tuberculiniques: les malades ayant des clichés négatifs présentèrent un taux élevé de négativation; au contraire, aucune modification dans les réactions cutanées ne fut décelée quand les constatations radiologiques indiquaient une lésion "probablement active."

Chez des cobayes qui ont été traités par l'isoniazide, leurs réactions tuberculiniques diminuent en intensité comparativement à celles des témoins non soumis au traitement. Si le traitement est commencé au moment même de l'inoculation, quelques animaux ne présentent pas de réactions tuberculiniques positives, et tous donnent des cultures négatives. Si le traitement est différé, tous avaient des réactions cutanées tuberculiniques faibles, et un petit nombre d'entre eux présentent des manifestations de tuberculose à l'autopsie et à la culture.

ZUSAMMENFASSUNG

Es wurde ein bestimmter Prozentsatz von 160 Personen mit zuvor negativ gewesener Tuberculinreaction, die positiv geworden war, wiederum negativ, wenn sie durch wiederholte Teste weiter beobachtet wurde in direktem Verhältnis zum Ausmass des Reaktionsvermögens. 68 Personen einschliesslich Kleinkinder, die während ihres ersten Lebensjahres positiv waren, zeigten einen Umschlag von Positiv zu Negativ in 76%, sofern der Hauttest einfach positiv war, in 50%, wenn er zweifach positiv war, in 38% wenn er dreifach positiv war und nur ein Fall mit einer Reaktion von Stärke 4 zeigte einen Umschlag. Die Gründe für diese überraschend hohe Umschlagsrate sind unbekannt; aber es ist so die frühe Entdeckung der tuberkulösen Infektion bei Personen möglich, die sonts in diesem Stadium ihrer Erkrankung unerkannt bleiben. Durch wiederholte Testung bei bekannten negativen und positiven Personen lässt sich der natürliche Ablauf der Erkrankung besser verstehen.

Es liegt auch daran, dass weitere Prüfungen mit dem Tuberkulintest erforderlich sind, ehe man seine Bedeutung voll abschätzen kann. Röntgenologische Untersuchungen ergaben eine direkte Beziehung zwischen den Befunden und dem Ausmass des Wechsels in der Reaktionsfähigkeit auf Tuberkulin, in dem Patienten mit negativen Thoraxröntgenfilmen eine grosse Zahl von Reversionen aufwiesen.—Im Gegensatz dazu fand sich kein Wechsel in der kutanen Reaktionsfähigkeit in Fällen, in denen die Befunde auf einen "vermutlich aktiven" Herd hinwiesen.

Wurden infizierte Meerschweinchen mit INH behandelt, verringerte sich ihre Hautreaktionsfähigkeit im vergleich zu den unbehandelten Kontrolltieren. Wurde mit der Behandlung begonnen zu einem Zeitpunkt als die Impfung erfolgt war, kam es bei einigen Tieren zu keinerlei positiver Reaktion und alle wiesen negative Kulturen auf. Wurde die Behandlung jedoch verzögert, entwickelte sich bei allen Tieren eine schwache positive Hautreaktion, und einige wenige hatten Zeichen von Tuberculose bei der Autopsie und in der Kultur.

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Concealed Drainage of the Middle Lobe of the Lung into the Superior Vena Cava through a Tributary of the Superior Pulmonary Vein

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In Brody's classic summary of 106 cases of anomalous drainage of the lungs into the right atrium or its tributaries, the author distinguished the following three grades of aberrancy: I, Incomplete drainage of the lungs into the right heart; II, Complete drainage into the right heart; and III, Complete drainage into the right heart, with associated anomalies. A decade later, Healey ('52) raised the number of such cases to 147, of which 86 fell into the category of partial drainage. In 33 of these, one or more pulmonary veins emptied into the superior vena cava; in another 18 they emptied into the right atrium, and in another 19 into the left innominate vein. In Smith's comparable figures of 1952 the right pulmonary vein was displaced twice as frequently as the left and, in those cases in which the sex was recorded, nearly thrice as often in males as in females.

Thus the anomaly presented in this article falls into the commonest division of the most frequently occurring type—namely the drainage in a male of the right superior pulmonary vein into the superior vena cava. Nevertheless, it differs from any case hitherto recorded—so far as the authors are aware—in the concealed pattern of drainage of the middle lobe. Because of this, a surgeon viewing the hilum of the lung at the time of operation would form an erroneous estimate of how much oxygenated blood was being dissipated into the right heart.* Accordingly, it has seemed desirable to record this case.

The specimen presented in figures 1 and 2 was obtained from the cadaver of a white man who died at the age of 67. The death certificate gave the cause of death as a cerebral vascular occlusion.

The figures indicate that in the right lung there are two pulmonary veins having approximately equal cross sections. The right inferior emptied normally into the left atrium just above the upper end of the pulmonary ligament (fig. 1). This vein drained not only the entire right lower lobe but a portion of the middle lobe through a small tributary which joined the superior segmental vein, V^6. (See common stem of V^{5a} and V^{4b}, fig. 2.)

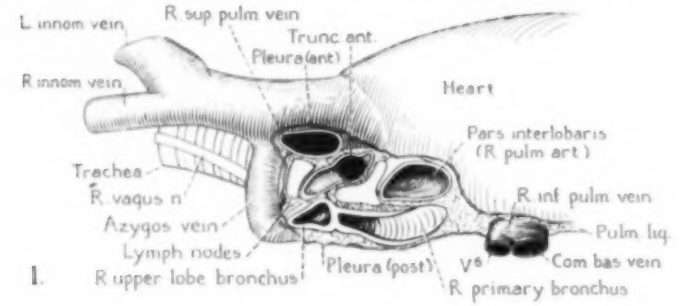
The right superior pulmonary vein terminated in the postero-lateral wall of the superior vena cava, just inferior to the entrance of the azygos vein (fig. 1). It drained the entire right upper lobe and, in addition, more than half of the middle lobe through an anomalous middle lobe vein

From the Department of Anatomy, University of Washington. Supported, in part, by research grant H-2547, Cardio-vascular Institute, National Institutes of Health.

*Parsons, Purdy and Jessup have estimated that unless 50 per cent or more of return flow from the lungs reaches the right heart no clinical symptoms will be produced. So, in the absence of these, or of catheterization, a surgeon would be guided, obviously, by what he could see, at the time of operation.

(VX^4, fig. 2). The deceptive feature was this hidden branch from the middle lobe. This is a sizeable vessel which begins peripherally between the costal surface of the middle lobe and the bronchi of the lateral segment, then enters the upper lobe deep to the anterior bronchus (B^{2b}) from which segment it receives a tributary (V^{2b}). It then joins the apical-anterior veins (V^1 and V^2) in the depths of the upper lobe.

The most recent explanation of anomalous drainage of the pulmonary veins into derivatives of the right or left common cardinal system, or into the right atrium or into the umbilico-vitelline system, is that presented by Catherine A. Neill ('56). Her figures, based upon reconstructions of young human embryos of the Carnegie Collection having a crown-rump



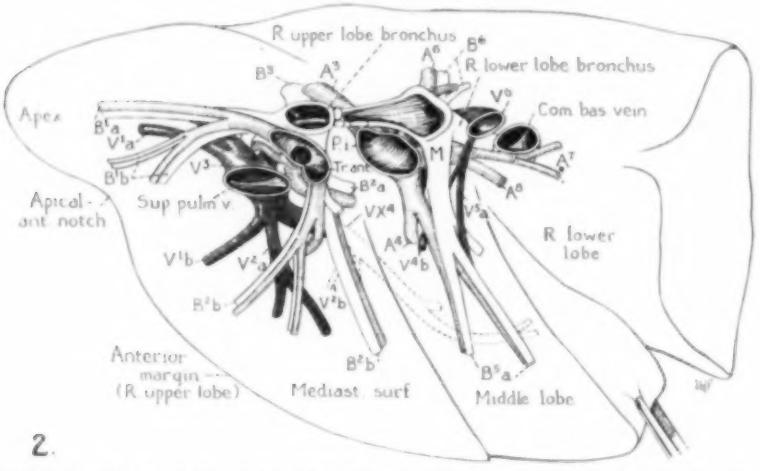


FIGURE 1: Sketch of the right side of the mediastinum of the cadaver of a 67 year old man showing the termination of an anomalous right superior pulmonary vein in the superior vena cava (X ½).

FIGURE 2: Dissection of right lung of same cadaver (X ½) illustrating the course of the concealed vein (VX^4) from the lateral segment of the middle lobe. B^1, B^2, B^3, apical, anterior and posterior bronchi of right upper lobe; A^1, A^2, A^3, and V^1, V^2, V^3, corresponding arteries and veins of upper lobe segments; B^4, B^5; A^4, A^5 and V^4, V^5, bronchi, arteries and veins, respectively, of the lateral and medial segments of the middle lobe; M, middle lobe bronchus. The middle lobe has been drawn to one side to expose root structures of the right lower lobe. V^6 and *Com. bas. v.*, chief tributaries of right inferior pulmonary vein. (For other designations, see Boyden, '55.)

length of 4 to 7 mm. show the close juxtaposition of the pulmonary plexus to the horns of the sinus venosus, the surrounding systemic veins and the visceral plexus. Drainage of the right pulmonary vein into the superior vena cava represents a persistence of early communications between the pulmonary venous plexus and the right horn of the sinus venosus coupled with a failure in the development of the right pulmonary vein.

The origin of the concealed tributary from the middle lobe is a later development and results from the persistence of atypical channels in the venous plexus of the growing middle lobe. The one shown in figure 2 (VX^1) is a variant of the type which drains the middle lobe superiorly instead of medially (cf. V^{1a}, fig. 51 and VX^{1a}, spec. no. 50, fig. 47, Boyden, '55).

SUMMARY

A unique variation of anomalous drainage of the right superior pulmonary vein into the superior vena cava has been presented. Through a large concealed tributary, much of the blood from the middle lobe passes into the superior pulmonary vein which otherwise drains the upper lobe into the vena cava. Consequently, half of the blood from the right lung passes into the right atrium. Because of the concealed course of the middle lobe vein, more oxygenated blood enters the vena cava than would have been anticipated from surgical examination of the hilum.

RESUMEN

Se presenta una variación singular de canalización anómala de la vena pulmonar superior derecha hacia la vena cava superior. Por intermedio de una tributaria grande oculta much sangre del lóbulo medio pasaba hacia la vena pulmonar superior que por otra parte, vierte la sangre del lóbulo superior dentro de la cava. Por consecuencia, la mitad de la sangre del pulmón derecho ingresa al atrium derecho.

A causa del curso oculto de la vena del lóbulo medio más sangre oxigenada ingresa a la cava de lo que prodía esperarse según el examen quirún del hilio.

RESUME

Les auteurs rapportent un cas unique de drainage anormal de la veine pulmonaire supérieure droite dans la veine cave supérieure. Par un large affluent occulte, la plupart du sang provenant du lobe moyen passe dans la veine pulmonaire supérieure qui autrement draine le lobe supérieur dans la veine cave. En conséquence, la moitié du sang provenant du poumon droit passe dans l'oreillette droite. A cause du cheminement caché de la veine du lobe moyen, entre dans la veine cave une plus grande quantité de sang oxygéné que ce qu'on aurait pu penser d'après l'examen chirurgical du hile.

ZUSAMMENFASSUNG

Eine einzigartige Variation einer anormalen Drainage der rechten Oberen Lungenvene zur oberen Hohlvene wird vorgestellt. Durch einen grossen verborgenen Nebenschluss gelangt ein erheblicher Teil des Blutes aus dem Mittellappen in die obere Lungenvene, die anderweitig den Oberlappen mit der vena cava verbindet. Infolge dessen gelangt die Hälfte des Blutes aus der rechten Lunge in den rechten Vorhof. Wegen des verborgenen Verlaufs der Mittellappenvene gelangt mehr Sauerstoffhaltiges Blut in die vena cava, als man nach der chirurgischen Untersuchung des Hilus hätte erwarten sollen.

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Congenital Hypoplasia of the Middle Lobe of the Lung, with Displacement of the Anterior Basal Bronchus to the Middle Lobe Stem

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In the typical right lung the middle lobe lies wedged between the anterior segment of the upper lobe and the anterior basal segment of the lower lobe. It is not surprising, therefore, that in rare instances the bronchus of the middle lobe should arise in common with one or the other of these contiguous bronchi. Various types of union with the anterior segmental bronchus have been discussed by Boyden, '55 (p. 43 and 47), but, as yet, only one instance of union with the anterior basal segmental bronchus has come to the writers' attention. This was a case of Huizinga's, cited by Esser ('57). The latter also notes that Narath found such an arrangement in the Orang.

The specimen illustrated in figure 1 was discovered in a man who had died from a brain tumor at the age of 60. The middle lobe was flattened to the thickness of a pancake and was hypoplastic.* Its horizontal surface was completely fused to the anterior segment of the upper lobe. Its surface on the oblique fissure was fused, toward the hilum, with what turned out to be the anterior basal segment, but the latter was separated from the rest of the lower lobe by a deep supernumerary fissure (cf. Smith and Boyden, '49, Plate 4).

Dissection of the specimen revealed the fact that a displaced anterior basal bronchus (BX^8, figure 1) was the principal branch of the middle lobe bronchus. The keel separating the middle from the lower lobe bronchus was normal in position, lying 2.8 cm. below the keel of the upper lobe bronchus. A view of the lower lobe bronchus such as one would see through a bronchoscope (insert, figure 1) showed that the orifice of the anterior basal segment is absent. When the middle lobe bronchus was cut open, it was found that it divided, 1.5 cm. from the keel, into a smaller common stem for the stunted medial and lateral bronchi of the middle lobe and a much larger anterior basal bronchus. The artery to this bronchus (A^8) arose from the basal artery in its usual position, notwithstanding the anomalous origin of the bronchus. However, the corresponding vein (VX^8) after receiving a middle lobe vein (V^5) emptied into the superior pulmonary vein (See arrow). The small middle lobe artery ($A^{5 \text{ and } 4}$) is the first branch of the basal artery. A^8 arises a short distance under $A^{5 \text{ and } 4}$; then the basal artery divides into A^9 and $A,^{10}$ with A^7 coming off of $A.^9$

Embryologically, this anomaly may be explained as follows: For some

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*Two of the University pathologists have stated that the microscopic appearance of a section taken through the full thickness of the middle lobe is compatible with the diagnosis of hypoplasia. Bronchial and vascular elements are present with little evidence of alveoli.

unknown reason, the bronchial bud which was to have given rise to the anterior basal segment arose from the middle lobe bronchus instead of from the basal trunk of the lower lobe. It then became the principal branch, thereby crowding the middle lobe branches against the upper lobe. As a result, the horizontal fissure failed to develop. Then because of the ectopic position of the anterior basal bronchus, a fissure developed between it and the rest of the lower lobe.

From a practical standpoint, the deceptive feature of this case would have been the normal bronchoscopic appearance of the carina separating

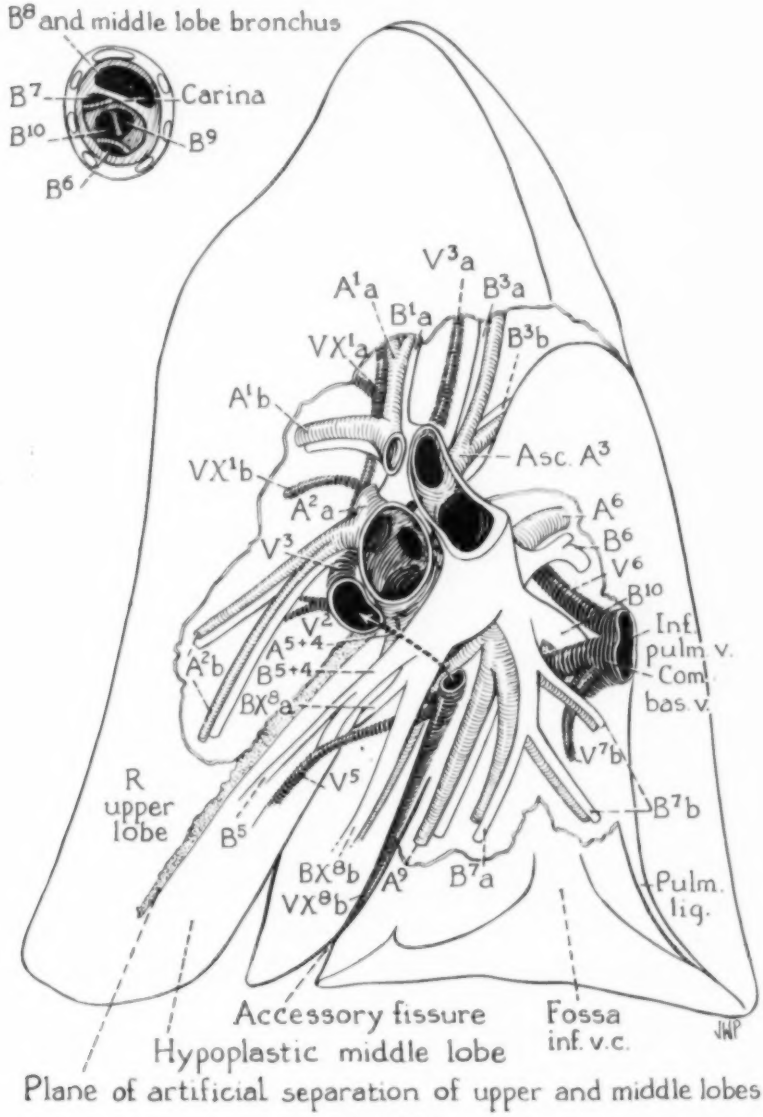

FIGURE 1

what would seem to be the bronchus of the middle lobe from that of the lower lobe. The absence of the orifice of the anterior basal bronchus would be accounted for normally on the basis that it was a displaced branch of B^9 (Ferry and Boyden, '51). If a bronchogram had been available it would have taken a keen observer to have distinguished between the displaced anterior basal bronchus and the segmental bronchi of the middle lobe.

Explanation of Figures

Figure 1: This sketch shows the mediastinal surface of the right lung of a 60-year old man in which a flattened hypoplastic middle lobe is fused congenitally to the right upper lobe. What appears to be the usual middle lobe trunk forks unexpectedly into a small abortive middle lobe bronchus (B^{5+4}) and a large displaced anterior basal segmental bronchus (BX^8). The latter is distributed to a lobe which is separated from the right inferior lobe by a supernumerary fissure. The artery of the stunted middle lobe (A^{5+4}) arises normally from the pars interlobaris of the right pulmonary artery, but the vein of the middle lobe (V^5) is a tributary of a displaced anterior basal vein ($VX^8a + b$) which joins the veins of the upper lobe (V^{1-3}) to form the superior pulmonary.

The *insert* is a bronchoscopic-like view of the main bronchus below the level of the upper lobe bronchus. Note the absence of the orifice of the anterior basal bronchus in the lower lobe stem. Its displaced position in the middle lobe stem is too deep to be seen in this view. (For other designations see Boyden, '55.)

SUMMARY

A rare case is presented in which the principal branch of a normally appearing middle lobe bronchus was found to be a displaced anterior basal segmental bronchus. The segment formed by the latter was partially fused to the stunted middle lobe near the hilum but was separated from the lower lobe by a deep supernumerary fissure. The hypoplastic segments of the middle lobe formed a flattened layer of tissue which was fused congenitally to the upper lobe.

RESUMEN

Se presenta un caso raro en el que la rama principal de un bronquio del lóbulo medio, de apariencia normal, era en realidad un bronquio segmentario anterior basal. El segmento formado por él estaba parcialmente en fusión con el lóbulo medio desmedrado cerca del hilio pero estaba separado del lóbulo inferior por una fisura supernumeraria profunda. Los segmentos hipoplásticos del lóbulo medio formaban una capa aplanada de tejido que se fusionaba congenitamente con el lóbulo superior.

RESUME

Les auteurs présentent un cas exceptionnel dans lequel la bronche qui semblait être la bronche principale du lobe moyen était en réalité la bronche du segment antérieur basal en position anormale.

Le segment formé par cette dernière était partiellement fusionné au lobe moyen rétracté près du hile, mais était séparée du lobe inférieur par une profonde scissure surnuméraire. Les segments atrophiés du lobe moyen formaient une couche aplatie de tissu qui était congénitalement fusionnée avec le lobe supérieur.

ZUSAMMENFASSUNG

Es wird berichtet über einen seltenen Fall, bei dem sich fand, dass der Hauptast eines normal erscheinenden Mittellappenbronchus ein verdrängter anteriorer basaler Segmentbronchus war. Das durch den letztgenannten gebildete Segment war zum Teil mit dem verkümmerten Mittellappen nahe dem Hilus verbunden, war jedoch vom Unterlappen durch eine tiefe überzählige Fissur getrennt. Die hypoplastischen Segmente des Mittellappens bildeten eine abgeflachte Bindegewebesschicht, die congenital mit dem Oberlappen verbunden war.

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Chronic Fibrous Mediastinitis and Superior Vena Caval Obstruction Due to Histoplasmosis

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Superior vena caval obstruction has been alleged to be caused by a wide variety of pathological conditions, some rather common and specific while others are relatively rare and indeterminate as to etiology. This troublesome syndrome was first described clinically by William Hunter 200 years ago according to McCord et al.[1] In their excellent review, McIntire and Sykes[2] cite that Fischer's series of 252 cases, reported prior to 1904, was comparable as to symptomatology and prognosis to the 250 cases appearing in the literature from 1904-1946.

Superior vena caval obstruction related to chronic fibrous mediastinitis was uniformly felt to be due to tuberculosis or syphilis until about 35 years ago. Surgical or autopsy verified cases of idiopathic fibrous mediastinitis have been reported with increasing frequency since that time.[2-15] Improvement in diagnostic technic of syphilis and tuberculosis were felt responsible for this change. The possibility of considerable diagnostic error was noted, particularly in earlier cases.[2]

In the verified cases of chronic fibrous mediastinitis reported, a granulomatous lymph node has frequently been associated with the process and occasionally has contained calcium.[2-4, 10, 12, 13, 15, 16] Other clinical cases have also shown this relationship.[1, 17-19] A diagnosis of tuberculosis has occasionally been made on the basis of these findings, however, when a specific statement has been made about microscopic findings of caseous granulomas, acid fast bacilli have not been demonstrated.[4, 5, 13] The unreliability of tissue etiologic diagnosis without demonstration of organisms has been well documented by Puckett.[20]

In 1925 Knox[3] noted that other agents which produce granulomata, such as the mycoses, might be the cause of fibrous mediastinitis. As late as 1956 Gillespie[16] suggested that upper an lower respiratory infections, bronchopneumonia, influenza, tularemia, trauma, rheumatic fever, and a tendency to form keloids might be implicated in chronic fibrous mediastinitis.

Gillespie[16] reported the case of a seven-year-old girl from a rural community of southern Illinois who developed superior vena caval obstruction in 1954, three and one half years after "virus-pneumonia." Chest roentgenogram showed multiple areas of fibrosis and calcification in both lung fields, rather marked infiltration or fibrosis in the upper two thirds of the right lung and pleural thickening along the right upper mediastinum. Blood serum complement fixation for histoplasmosis was 1:64 (yeast phase antigen). The histoplasmin skin test was strongly positive, but the old

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tuberculin 1:1000 was negative. A clinical diagnosis of pulmonary and mediastinal histoplasmosis was made. The child was referred to Vanderbilt University Hospital where right thoracotomy revealed massive leathery fibrosis of the mediastinum and thrombosis of the superior vena cava and azygos vein. Unroofing and partial phlebolysis of the incompletely occluded vena cava provided symptomatic relief from superior caval obstruction. Histoplasma capsulatum could not be demonstrated in the fibrous tissue submitted for histologic study. We are in complete concurrence, however, with the clinical diagnosis of mediastinal histoplasmosis.

During the past two years we have observed four similar cases at Fitzsimons Army Hospital which are felt to be secondary to histoplasmosis. These cases are the basis for this report as it is felt that histoplasmosis has an important place in the etiology of "idiopathic" chronic fibrous mediastinitis, and may be responsible for many such cases previously considered to be of tuberculous etiology.

Case 1: This 27 year old Negro was in good health until 1952 when he had a sore throat and coughed up bright red blood. He was then asymptomatic until May, 1956 when a similar episode occurred followed by blood-streaked sputum for about 18 hours.

On May 16, 1956 he was admitted to Fitzsimons Army Hospital. Physical examination was normal. Chest roentgenogram showed a homogenous spherical density four centimeters in diameter which involved the anterior segment of the left upper lobe. In 10 days there was complete resolution of this process. The white blood cell count and sedimentation rate were normal. Skin tests revealed PPD No. 2 positive, coccidioidin 1:100 negative and histoplasmin 1:100 positive. Three gastric cultures for *M. tuberculosis* were negative. Bronchoscopy was normal. Esophagoscopy revealed extensive vascularity of the esophagus but no other abnormality. He was returned to duty July 5, 1956.

On March 1, 1957 he had hemoptysis lasting about 24 hours and was rehospitalized for further evaluation.

Residence History: He was born in Missouri and had been stationed during military service in Kansas, Kentucky, California, Japan, Nebraska, Ohio, Wyoming, Massachusetts and Colorado.

Physical examination on re-admission was normal. White blood cell count and differential were normal. Chest roentgenogram March 5, 1957 revealed a five centimeter, soft, spherical infiltration in the anterior segment of the left upper lobe with an increase in the markings in the lingula (Figs. 1A and 1B). Within 10 days the pulmonary infiltration cleared. Bronchoscopy showed only hemorrhagic mucosa of the left upper

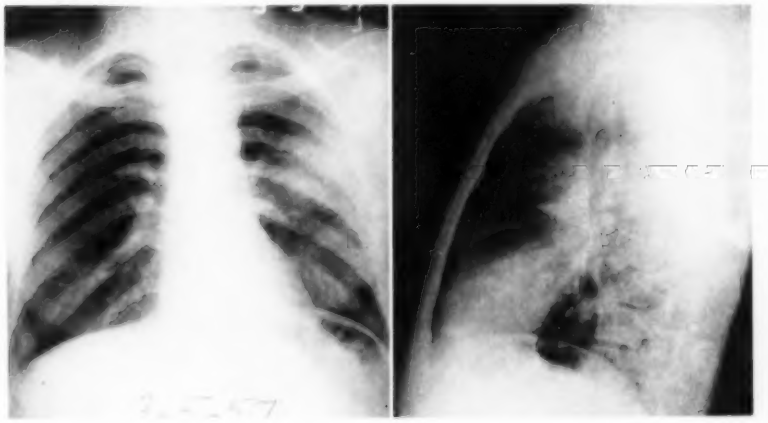


FIGURE 1A FIGURE 1B

Figure 1 (Case 1): (A) PA and (B) left lateral chest roentgenogram showing spherical infiltration in the anterior segment of the left upper lobe.

FIG. 2A

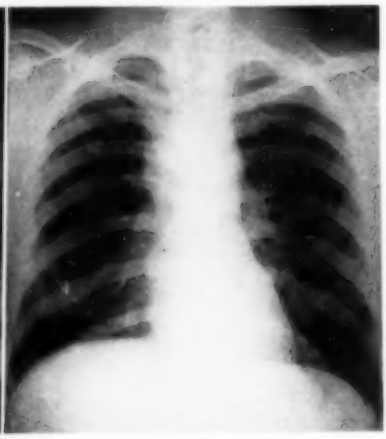
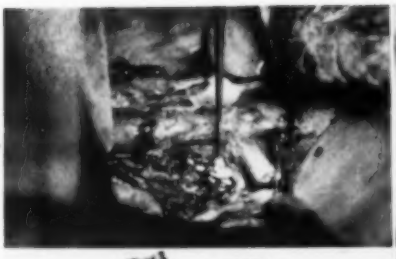


FIG. 2B

FIG. 2C



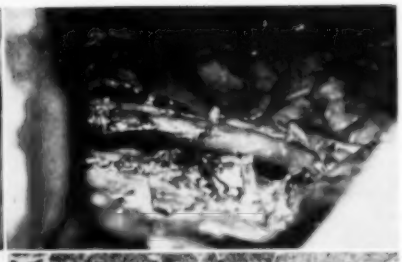
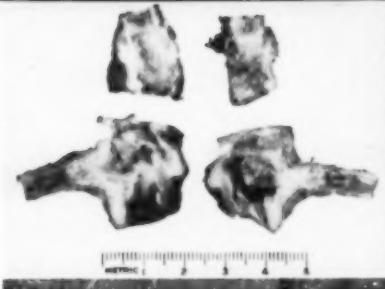


FIG. 2D

FIG. 2E



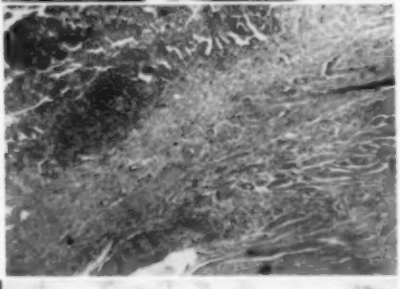


FIG. 2F

FIG. 2G

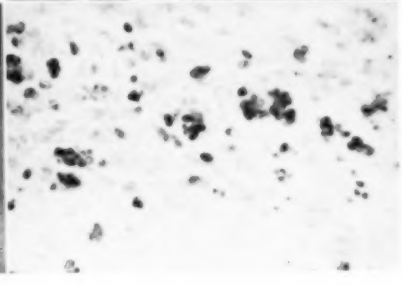


FIG. 2H

lobe bronchus. A left scalene lymph node revealed reactive hyperplasia. Serologic studies for fungi revealed:

Histoplasmosis	May 28, 1957	June 26, 1957	August 20, 1957	September 24, 1957
YP Antigen	0	0	0	0
MF Antigen	1:64	1:64	1:64	1:64
Colloidion agglutination	0	0	0	0
Blastomycosis	0	1:8	1:8	1:8
Coccidioidomycosis	0	0	0	0

On review of the serial roentgenograms slight enlargement of the left superior mediastinum was noted. Exploratory thoracotomy was recommended because of recurrent hemoptysis and pulmonary infiltration which was thought to be secondary to a lesion in the segmental bronchus, possibly a bronchial adenoma.

On April 5, 1957 left thoracotomy was performed. Thick adhesions from the inferior edge of the upper lobe to the chest wall and pericardium were found. Upon freeing these adhesions and opening the fissure, the bronchus to the lingula appeared to be involved in a hard mass, however, the lung was normal to palpation. A similar thick fibrous mass surrounded the pulmonary artery to such an extent that it could not be exposed. Further exploration revealed complete involvement of the great vessels arising from the arch of the aorta in a similar block of almost stony hard material that extended down into the aortic window. Biopsy material was obtained by excising thick fibrous tissue overlying the aortic arch and from the area between the aortic arch and the pulmonary artery, and a subcarinal lymph node.

Pathology: One specimen consisted of a plaque of extremely firm, fibrous, connective tissue measuring 5.5 x 2.5 x 0.6 centimeters in greatest dimensions. One surface was soft and congested, while the other surface was yellowish-gray and nodular. The cut surface presented a homogeneous pink fibrous appearance. Submitted separately was an irregular fragment of anthracotic lymphoid tissue, measuring 1.3 centimeters in diameter occupied centrally by a 4.0 mm. nodule of partially calcified caseous material. Sections revealed remarkably dense swollen avascular collagenous tissue infiltrated by moderate numbers of plasma cells and occasional lymphocytes. Sections of the partially calcified, necrotic material revealed organisms strongly suggestive of histoplasma capsulatum. The periphery of the nodule showed only hyalinized fibrous connective tissue without any recognizable cellular activity.

Course Since Surgery: He has been asymptomatic since thoracotomy seven months ago.

Case 2: This 25 year old white man was well until December 1, 1956 when he dates the onset of weakness, lethargy, and increasing pressure sensations in his head. About January 28, 1957 he developed swelling of his neck. He was hospitalized February 7, 1957 after several episodes of syncope and it was noted that he had lost 10 pounds in weight. Physical examination revealed swelling of the face, neck and upper extremities, marked conjunctival and oropharyngeal suffusion, papilledema and marked venous engorgement of the upper extremities, anterior and posterior chest wall, and neck (Fig. 2A). Moderate lymphadenopathy of the anterior and posterior cervical chain and axilla lymph nodes were noted. Because of the superior vena caval obstruction he was transferred to Fitzsimons Army Hospital.

His past history was non-contributory.

Residency History: He was born and reared in Minnesota. He received basic training at Fort Leonard Wood, Missouri, in 1954 and had been serving Alaska until his present illness.

Chest roentgenograms on admission (Fig. 2B) revealed a right superior mediastinal mass 3 centimeters in diameter projecting anteriorly as seen in the left anterior oblique projection, but not visualized as a tumor on lateral view.

Laboratory studies revealed normal complete blood count, urinalysis, and liver function studies. He did not react to No. 2 PPD or coccidioidin but was 2+ to 1:100

Figure 2: (A) Infrared photograph before surgery showing engorgement of collateral veins of neck, thorax and arms. (B) Chest roentgenogram showing the right peritracheal mediastinal lesion. (C) Superior vena cava in situ with transection of the azygos vein showing complete occlusion of the lumen. (D) Homologous aortic graft in situ at completion of anastomosis of the right innominate vein to the auricle. (E) Hemisection of the superior vena cava and azygos vein showing fibrous occlusion of the lumen. The upper fragment is the superior vena cava at the junction with the left innominate vein showing marked mural thickening. (F) Characteristic keloidal fibrous tissue with pulmonary, pleural and neural involvement. (G) Wall of the caseating granuloma in the peritracheal lymph node imbedded in fibrous tissue. (H) Characteristic organisms of *H. capsulatum* demonstrated in caseous material by Gomori silver methenamine stain.

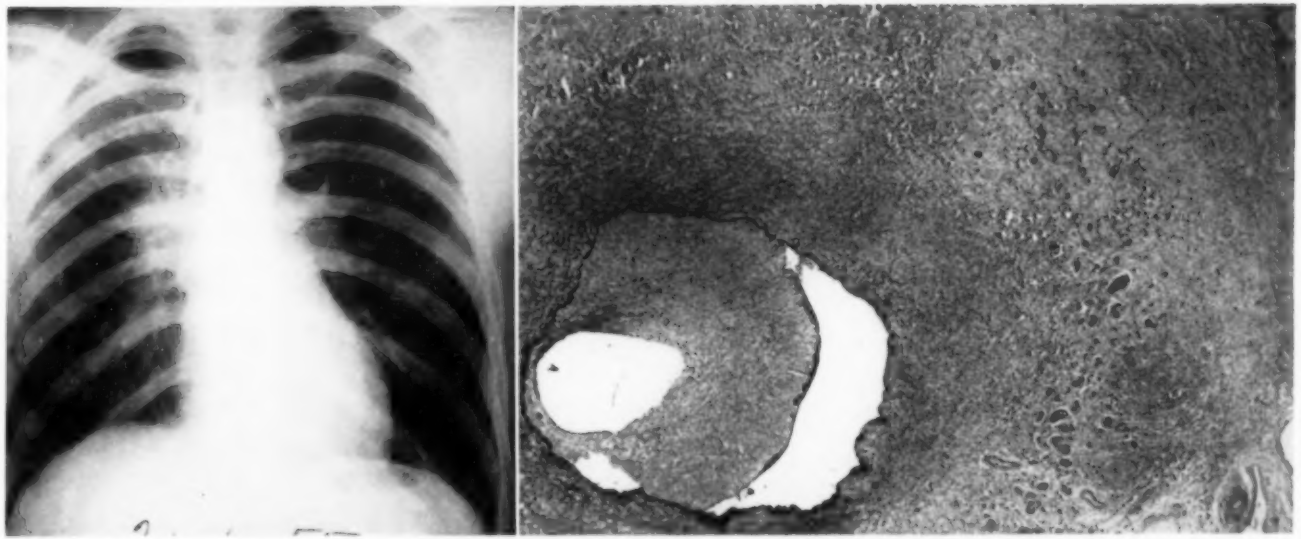


FIGURE 3A FIGURE 3B

Figure 3 (Case 3): (A) Chest roentgenograms showing the right hilar mass with linear and nodular infiltration of the right upper lobe. (B) Branch of the pulmonary artery showing marked disruption of the wall by collagenous fibrous tissue and mature thrombus formation.

histoplasmin. The venous pressure in both arms was 44 centimeters of saline. Serological studies for fungi revealed:

Histoplasmosis	April 11, 1957	June 18, 1957	September 3, 1957	October 9, 1957
YP Antigen	1:16	1:8	1:16	1:32
MF Antigen	1:128	1:16	0	1:8
Colloidion agglutination	0	0	equiv	equiv
Blastomycosis	1:8	0	0	0
Coccidioidomycosis	0	0	0	0

He was presented to the Tumor Board, where it was felt that this was probably a lymphoma and exploratory thoracotomy recommended. On March 25, 1957 right thoracotomy revealed extensive venous collaterals in the thoracic wall. On opening the chest, the lung appeared and felt normal. In the superior aspect of the right hilar region, there was a fixed, hard mass about 7.5 centimeters in diameter involving the mediastinum, the azygos vein, superior vena cava, the left innominate vein, the trachea and right bronchus. A biopsy was taken from the angle between the superior vena cava and azygos vein. Below a 6 to 8 mm. fibrous capsule was a conglomerate, caseating mass which had the appearance of granuloma (Fig. 2C). There was no evidence of neoplasm. As the great vessels were dissected it was apparent that the azygos vein was completely fibrotic and thrombosed and that this mass involved the wall of the superior vena cava, causing complete obliteration at the level of an azygos vein. The process extended from the pericardium to the right innominate vein. The phrenic nerve was bound down in the fibrous mass. The azygos vein and superior vena cava were excised and the vena cava replaced from the right innominate vein to the auricle by an aortic homograft (Fig. 2D).

Pathology: The surgical specimen was received in two portions (Fig. 2E); the largest consisted of the inferior portion of the superior vena cava and the azygos vein. The internal diameter of the superior vena cava visualized inferiorly was 1.0 centimeter but was funnel-shaped and occluded by firm fibrotic thrombus. The superior aspect of this specimen presented an irregular lumen 6.0 mm. in diameter. Longitudinal hemisection revealed that the lumen of the terminal segment of the azygos vein was completely obliterated by a firm thrombus. This thrombus was firmly attached to the indurated wall and extended irregularly into the superior vena cava, merging with the previously described lesion. The upper fragment of the superior vena cava revealed similar mural thickening composed of avascular fibrous connective tissue upon the inner aspect of which there was a similar thrombus. Microscopic sections of all tissue presented a homogeneous, sclerotic, collagenous tissue extending irregularly around and through all structures observed (Fig. 2F). There was a moderately-heavy, chronic inflammatory cell infiltrate consisting primarily of plasma cells with minimal numbers of lymphocytes and occasional eosinophiles. Multiple sections failed to reveal any evidence of a specific granulomatous process.

The lymph node removed from the tracheal chain showed an inspissated caseous granuloma surrounded by keloidal fibrous tissue (Fig. 2G). Gomori silver methenamine stains of the caseous material revealed morphologically typical organisms of histoplasma capsulatum (Fig. 2H). Acid-fast stains were negative.

Course Since Surgery: Immediately following surgery relief of the superior vena caval obstruction was evident with complete disappearance of the edema of the upper extremities, head, and neck and a fall in the venous pressure in the upper extremities. Five months later, however, swelling of the head, neck, and arms reappeared but has not progressed to the extent seen prior to thoracotomy.

Angiography now reveals complete obstruction of the right innominate vein and reconstructed superior vena cava. At present, eight months, after thoracotomy, it is quite obvious that more extensive venous collaterals are present over the lateral and anterior aspects of the chest as well as over the superior and inferior epigastric regions. Elevation of the head of his bed is not required, and he is relatively asymptomatic except with vigorous physical activities. Additional reconstructive vascular surgery does not appear warranted or feasible.

Case 3: This 30 year old white man was well until May, 1955 when he began losing weight without apparent cause. About three weeks later, while flying at 30,000 feet, he experienced sudden shortness of breath, slight substernal chest pain, and non-productive cough attributed to decompression. However, the symptoms continued and on June 14, 1955 he was hospitalized at Barksdale Air Force Base because of a chest roentgenogram showing right hilar enlargement. Histoplasmin, PPD Nos. 1 and 2 skin tests were negative but O.T. was questionably positive. Sputum examinations were negative. All symptoms subsided and he was returned to duty June 27, 1955. On July 8, 1955 he first noted hemoptysis with continued blood streaking for five days. A chest roentgenogram revealed an increase in the right hilar mass and resulted in his evacuation to Fitzsimons Army Hospital for further observation.

His past history was non-contributory.

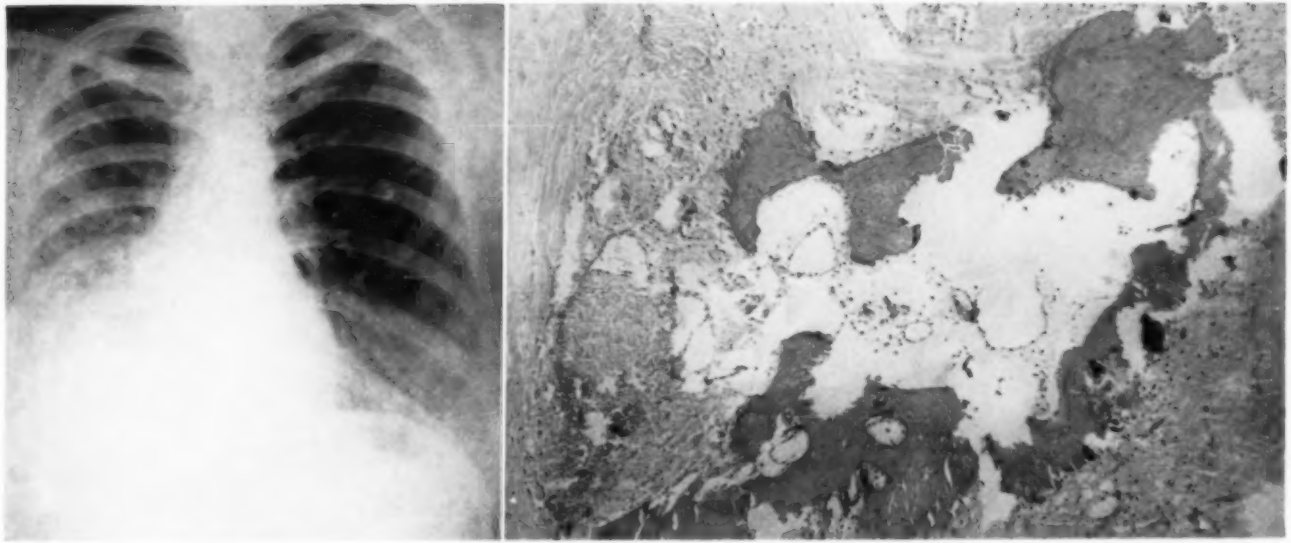


FIGURE 4A FIGURE 4B

Figure 4 (Case 4): (A) Chest roentgenogram July 18, 1955 showing right pleural thickening, enlargement of a lymph node about the bronchus intermedius and collapse of the right middle lobe. (B) Osseous metaplasia of mediastinal fibrous tissue obtained at second thoracotomy.

Residence History: He was born in Michigan, travelled through the United States, and had lived several years in northwestern Louisiana preceding his illness.

Physical examination revealed a well-nourished, well-developed man who appeared in good health. Mild generalized non-tender lymphadenopathy was present. A few fine rales were heard in the right midlung field posteriorly. A grade-II, apical systolic cardiac murmur was heard.

Admission chest roentgenogram (Fig. 3A) revealed soft nodular and linear infiltrations of the right upper lobe and marked prominence of the right hilar and peritracheal area.

Laboratory studies showed a normal complete blood count, urinalysis and cardiolipin. Numerous sputum cultures were negative for *M. tuberculosis* and pathogenic fungi. Skin tests: Histoplasmin 1:1000 2+ (conversion), PPD Nos. 1 and 2, coccidioidin negative. Serological studies for fungi revealed:

	July 25, 1955	September 3, 1955	September 20, 1955	March 23, 1956
Histoplasmosis	1:16	1:16	1:16	neg
Colloidion agglutination	1:8	1:16	neg	neg
Blastomycosis	neg	neg	neg	neg
Coccidioidomycosis	neg	neg	neg	neg

Course in Hospital: Bronchoscopy was normal and bronchial washings negative for fungi, *M. tuberculosis* and tumor cells. Scalene node biopsy showed reactive hyperplasia. Exploratory thoracotomy October 26, 1955 revealed marked vascular adhesions over the posterior portion of the right upper lobe, necessitating retropleural dissection. A large tumor-like mass was found in the hilum, involving all structures, predominately around the upper lobe. A further tumor-like mass found in the anterior segment measured 2.5 x 4 centimeters. The mediastinal mass extended to include the superior vena cava from the pericardium approximately eight centimeters superiorly. The main stem pulmonary artery, bronchus, the lower trachea, and the superior pulmonary vein were included in the mass. Biopsy of the posterior mediastinum revealed fibrous tissue with acute and chronic inflammatory reaction. Further dissection showed occlusion of the pulmonary artery branch to the posterior segment of the right upper lobe by the tumor-like mass; this was removed as a biopsy specimen. The azygos vein was similarly completely occluded and excised without bleeding. The fibrotic process also involved the contiguous pericardium and the superior and lateral wall of the right atrium. Venous pressure in the superior vena cava above the obstruction was 26.5 centimeters of saline. An enlarged hilar node was removed and the procedure terminated since individual dissection and ligation of structures preparatory for right upper lobectomy were impossible.

Pathology: The specimen consisted of tissue removed from the right lung, the pleura, the mediastinum and the azygos vein. Sections revealed a marked fibrous connective tissue process of a predominately mature pattern with foci of fibroblastic activity (Fig. 3B). This was infiltrated by moderate to marked numbers of plasma cells and occasional lymphocytes and eosinophiles without respect to anatomic boundaries such as pleura, fascia or vein. No granulomatous disease was observed. The mediastinal lymph node showed only reactive hyperplasia.

Course Since Surgery: He was returned to limited duty January 10, 1956 but failed to regain weight, tired easily, had recurrent anterior chest pain, productive cough, and hemoptysis. He was rehospitalized March 17, 1956 when examination revealed generalized mild lymphadenopathy, decrease in breath sounds over the upper chest bilaterally, and occasional wheezing over the left upper lobe area. A pericardial friction rub was noted for two weeks. Multiple lymph node biopsies showed reactive hyperplasia.

He was temporarily retired with a diagnosis of "Fibrosis, proliferation of lung, mediastinum, superior vena cava, azygos vein, pericardium and right auricle of heart, chronic, progressive, of unknown cause."

Since April 1956 although he has remained active he has had recurrent anterior chest pain and pulmonary hemorrhage about every two to three weeks requiring hospitalization on three occasions. In September, 1957 he was permanently retired.

Case 4: This 30 year old white woman was admitted to Fitzsimons Army Hospital March 11, 1955 having first been hospitalized November 22, 1954 at the United States Army Hospital, Regensburg, Germany.

Her illness began November 18, 1954 with chills, fever, and hacking non-productive cough. Two days later she began having right pleuritic chest pain and was hospitalized.

Chest roentgenogram showed right pleural effusion. White blood cell count was 10,150 with normal differential distribution. Thoracentesis November 26, 1954 yielded about 500 cc. straw-colored fluid with specific gravity of 1.017 and cell count of 1,700 WBC, 61 per cent lymphocytes and 39 per cent neutrophils. The pleural fluid was reported as showing an occasional acid-fast bacillus however culture was negative for *M. tuberculosis*. Skin tests: PPD No. 2 and coccidioidin were negative but histoplasmin was 3+. She was transferred to Fitzsimons Army Hospital March 11, 1955

with a diagnosis of tuberculosis pleurisy with effusion. Her past history was noncontributory.

Residence History: She was born in Mississippi and subsequently lived in Tennessee and Kentucky. Her only overseas station was in Germany from mid-1952 until returning to the States in March 1955.

Physical examination on admission was within normal limits except for slight decrease in vocal fremitus in the right base posteriorly and a few fine post-tussic rales in the same area.

Laboratory studies showed a normal complete blood count, urinalysis, and cardiolipin. Numerous gastric cultures were negative for *M. tuberculosis* and pathogenic fungi. Repeated skin tests confirmed the negative tuberculin and coccidioidin, but the histoplasmin was strongly positive. Chest x-ray film revealed persistent right pleural thickening and a mass in the right hilum associated with collapse of the right middle lobe (Fig. 4A).

Course in Hospital: Between February 1, 1955 and March 29, 1955 she had three episodes of hemoptysis. On the latter occasion she was bronchoscoped and blood was seen coming from the right lower lobe area. She was rebronchoscoped April 26, 1955 and severe stenosis of the bronchus intermedium was noted. The mucosa was granular, friable, shaggy-appearing and bled easily. The right middle lobe orifice could not be visualized. The secretions obtained by bronchoscopy were negative on culture for *M. tuberculosis* and on Papanicolaou's smear for malignancy.

Attempts to clear the severe endobronchial disease with antibiotics was unsuccessful until tracheostomy was performed to facilitate drainage from the right main stem bronchus. At thoracotomy, July 21, 1955, the entire right lung was densely adherent to the chest wall by multiple vascular adhesions. A hard, tumor-like mass was found involving the hilum, extending into the mediastinum and left hemithorax. As the posterior aspect of the hilum was freed the mass was found to "encase in a cement-like cast" both main stem bronchi, carina and about two centimeters of the lower trachea. Part of the "tumor" extended anteriorly and involved the lateral portion of the superior vena cava from the level of the azygos vein to its entrance into the right auricle subpericardially. The lower lobe felt as if there was extension into the lung parenchyma itself. The mass was adherent to the esophagus; the right pulmonary artery and vein were also grossly involved. Multiple biopsies of tissue removed from the right main stem bronchus, the wall of the superior vena cava and the lymph nodes from the superior mediastinum and near the carina were obtained.

Gross examination of the lymph nodes revealed complete loss of normal lymphoid architecture due to fibrosis. Examination of fragments of bronchus and superior vena cava showed dense homogeneous fibrous connective tissue without evidence of granulation tissue or caseation. Microscopic examination confirmed the gross impression of a mature dense fibrosing process involving the bronchial wall and the tissues about the superior vena cava. Sections of the lymph node showed fibrosis without evidence of specific granulomatous inflammation.

Following surgery repeated bronchoscopy was done in an attempt to dilate the bronchus intermedius. Due to failure of obtaining diagnostic tissue thoracotomy was

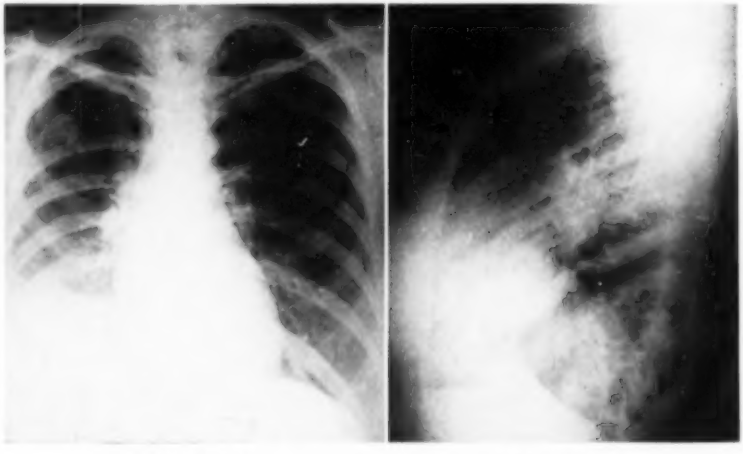


FIGURE 4C FIGURE 4D

Figure 4 (Case 4): (C) PA and (D) lateral chest roentgenograms January 24, 1957 showing pleural and pulmonary fibrosis and enlarged, partially calcified hilar lymph nodes.

repeated September 19, 1955. The right middle and lower lobes were markedly fibrotic and expanded poorly after decortication. Extensive further calcification of the mediastinal and hilar mass had occurred precluding definitive surgery. Generous biopsies were removed from the mediastinal pleura, the lung and right main stem bronchus. Grossly these were fragments of dense fibrous connective tissue showing on cut surface foci of dense calcification. Microscopic examination disclosed mature fibrous connective tissue with foci of marked fibroblastic activity accompanied by large numbers of lymphocytes, plasma cells and occasional eosinophils. No granulomatous inflammatory process was observed, and considerable osseous metaplasia was present (Fig. 4B).

The tracheostomy was repaired October 10, 1955 after repeat bronchoscopic dilatation of the bronchus intermedius relieved stenosis to about 20 per cent. She was discharged home October 15, 1955. On November 11, 1955 she was readmitted for treatment of mild serum hepatitis (19 pints of whole blood were given during previous surgery July and September, 1955), and discharged home December 17, 1955. In March, 1956 she began having cough productive of one-fourth cupful yellowish sputum daily. Bronchoscopy revealed moderately opaque mucosa of the right main stem bronchus which bled easily. Mild stenosis of the right upper, middle and lower lobe orifice was noted but little changed from six months before.

She has been well, doing full time work as a teacher since April, 1956. The most recent chest roentgenograms, February, 1957, reveal minimal fibrothorax and linear fibrosis of the right lower chest, and questionable increase in calcification of the hilar and mediastinal mass (Figs. 4C and 4D).

Discussion

It is doubtful that the incidence of the superior vena caval syndrome is decreasing because there is rather conclusive evidence that primary tumors of the lung are on the increase, and there are trends which cause us to believe that mediastinal tumors may likewise be increasing. Jaffe,[21] in a study of 100 necropsies with carcinoma of the lung, found that seven of the tumors had invaded and obliterated the superior vena cavae—all of these had developed extensive venous collaterals in the chest wall. There has been a remarkable decrease in the incidence of residuals of syphilis during the past 15 to 20 years; we must surmise, therefore, that syphilitic mediastinitis and aortitis which formerly gave clinical or pathologic evidence of superior vena caval obstruction is seldom seen.

It is our impression that the incidence of mediastinitis of most types is declining. The possible exception to this clinical impression is the extensive fibrosing mediastinitis now thought to be rather characteristic of histoplasmosis. There is indirect but presumptive evidence that pyogenic infections, in this antibiotic era, seldom result in symptomatic chronic mediastinitis.

Of 250 cases of superior vena caval obstruction reported between 1904 and 1946,[2] 62 (24.8 per cent) were due to chronic fibrous mediastinitis. Of these 62, 16 were considered to be idiopathic, 27 luetic and 19 tuberculous. During this period the number of cases reported as idiopathic chronic fibrous mediastinitis changed from none (1904-1921), to 5 per cent (1922-1933), to 11.7 per cent (1934-1946). Although this change may be related to efficacy of treatment of syphilis it seems probable that the change was due to a greater tendency of pathologists to report cases as idiopathic when proof of etiology was lacking.

A corollary, in this respect, seems to apply to tuberculous involvement of mediastinal nodes and structures. The clinical impression that tuberculosis rarely results in chronic fibrous mediastinitis and superior vena caval obstruction is based upon the following facts and assumptions: 1) earlier diagnoses and institution of highly effective antituberculosis therapy during the past decade; 2) tuberculosis control in dairy herds and almost universal pasteurization of dairy products in this country—a lim-

ited experience in the resection of pulmonary tuberculosis in foreign born women dependents of service men has often revealed a calcific hilar adenitis and angiitis more extensive than that seen in American patients but in no instance was there evidence of extensive mediastinal fibrosis[22]; 3) over 1200 patients have undergone pulmonary resections for proved tuberculous lesions at this hospital during the past 10 years without the surgeons finding any evidence of significant mediastinitis as portrayed by the four cases reported; neither have resected mediastinal lesions, solitary or multiple, which proved to be chronic tuberculous lymphadenitis been associated with massive mediastinal fibrosis or vena caval obstruction; 4) Auerbach[23] states that he has never demonstrated tuberculous mediastinitis producing superior vena caval obstruction.

The salient pathologic features of this disease appear to be a progressive evolution of remarkably dense sclerotic fibrous tissue characterized by swollen angular clumps of collagen alternating with fibrocytes. This description parallels the microscopic appearance of a cutaneous keloid, as noted by Knox.[3] The process displays a remarkable tendency to invade all structures with which it comes in contact without respect to anatomic boundaries. This "keloidal fibrous tissue" is accompanied by moderate numbers of plasma cells and lesser numbers of lymphocytes and occasional eosinophils. Osseous metaplasia is occasionally observed.

Proliferative collagenous replacement of lymph nodes renders histologic and cultural confirmation of histoplasma capsulatum difficult unless lymphoid tissue is obtained at thoracotomy prior to complete replacement of the granulomatous process with dense fibrous tissue. Buried within such lesions there may be found caseating granulomata which contain organisms typical of histoplasma capsulatum.

Clinicians, surgeons, and pathologists who have reviewed the literature and their clinical experiences with chronic fibrosing mediastinitis or superior vena caval obstruction since the turn of the century report that from 15 to 50 per cent of such lesions were secondary to chronic inflammatory diseases. Of the specific varieties, tuberculosis and syphilis always have been included or implicated; however, such diagnoses were often presumptive as unequivocal laboratory proof has only seldom been evident, excluding aortic aneurysms. In view of our present concepts of fibrosing mediastinitis, we propose that a significant percentage of such lesions considered in the past to be tuberculous, syphilitic, thrombotic, traumatic, rheumatic, cicatricial (keloid), or idiopathic in nature were actually due to the rather uniform response of the mediastinal lymph nodes and related anatomical structures to histoplasma capsulatum infection.

SUMMARY

Four patients, age 25 to 30 years, with bronchial or mediastinal venous obstruction due to chronic fibrous mediastinitis are reported.

Fibrous mediastinal lesions with various degrees of calcification were so extensive, obliterating anatomical planes, that pulmonary resections were technically impossible or considered unwise.

Clinical and laboratory findings with uniform gross and microscopic appearance of these intrathoracic lesions, in our opinion, has given us a sufficient basis to make a diagnosis of chronic fibrous mediastinitis due

to histoplasmosis. Morphologically typical organisms of histoplasma capsulatum were demonstrated in the caseous material from a granulomatous lymph node in one patient and organisms highly suggestive of such a fungus disease were found in another.

Multiple mediastinal biopsies from the other two patients were not conclusively diagnostic in that no lymph node demonstrating such early collagenous replacement of necrotic foci was encountered although the typical hyalinized fibrous and calcific tissue was in abundance.

Discussion points are presented dispelling the past opinions that severe chronic mediastinitis and associated superior vena caval obstruction may be the result of a tuberculous process.

RESUMEN

Se hace mención de cuatro enfermos de 25 a 30 años de edad con obstrucción venosa bronquial o bilateral debida a mediastinitis fibrosa crónica.

Las lesiones fibrosas mediastinales con varios grados de calcificación eran tan extensas y abliteraban planos anatómicos, que la resección pulmonar fué técnicamente imposible o considerada imprudente.

Los hallazgos clínicos y de laboratorio con apariencia macro y microscópica de estas lesiones intratorácicas, de acuerdo con nuestra opinión, nos dan base suficiente para hacer el diagnóstico de mediastinitis fibrosa crónica debida a histoplasmosis. Histoplasma capsulátum típico se encontró en el material caseoso de un ganglio granulomatoso en un enfermo, en otro se encontraron organismos que sugerían fuertemente una micosis.

Las biopsias múltiples de los otros dos enfermos no condujeron a diagnóstico concluyente, pues no se encontró ganglio alguno demostrando tan temprana substitución por colágena de los focos necróticos, aunque había tejido en abundancia hialinizado típico fibroso y tejidos calcificados.

Se discute y se descarta la opinión del pasado de que la mediastinitis severa crónica y la obstrucción de cava resultante puedan ser resultados de una afección tuberculosa.

RESUME

Les auteurs rapportent les observations de quatre malades, âgés de 25 à 30 ans, atteints d'obstruction veineuse médiastinale ou bronchique, imputable à une médiastinite fibreuse chronique.

Les lésions fibreuses médiastinales, présentant différents degrés de calcification, furent si extensives, oblitérant les plans anatomiques, que les résections pulmonaires furent techniquement impossibles, ou considérées comme inopportunes.

Les constatations cliniques et bactériologiques, montrant aussi bien macroscopiquement que microscopiquement l'existence des lésions intrathoraciques, ont donné aux auteurs des éléments suffisants pour faire le diagnostic de médiastinite fibreuse chronique, due à l'histoplasmose. Des germes morphologiquement typiques *d'histoplasma capsulatum* furent mis en évidence dans le caséum obtenu à partir d'un nodule granulomateux chez un malade, et des germes hautement évocateurs de cette mycose furent découverts chez un autre.

Des biopsies médiastinales multiples chez les deux autres malades ne

purent permettre de conclúsion car on ne put découvrir aucun ganglion avec la refonte collagène précoce des foyers nécrotiques bien qu'il y eut en abondance les aspects caractéristiques de tissu fibreux hyalin et de calcifications.

Les auteurs présentent les arguments qui détruisent l'opinion qu'on avait naguère selon laquelle la médiastinite chronique grave associée à l'obstruction de la veine cave supérieure pouvait être le résultat d'un processus tuberculeux.

ZUSAMMENFASSUNG

Bericht über vier Patienten im Alter zwischen 25 und 30 Jahren mit bronchialem oder mediastinalem Venenverschluss infolge chronischer fibröser Mediastinitis. Die fibrösen mediastinalen Herde mit verschiedenen Graden von Verkalkung waren so ausgedehnt mit Verschluss anatomischer Einheiten, dass Lungenresektionen technisch unmöglich waren oder als unzweckmässig angesehen wurden.

Befunde aus Klinik und Laboratorium mit einheitlichem makroskopischem und mikroskopischem Aussehen dieser intrathorakalen Veränderung haben uns unserer Auffassung nach eine genügende Grundlage geliefert, um die Diagnose einer chronischen fibrösen Mediastinitis infolge Histoplasmose zu stellen. Morphologisch typische Organismen von histoplasma capsulatum liessen sich in dem käsigen Material aus granulomatösen Lymphknoten bei einem Patienten nachweisen, und bei einem anderen Patienten wurden Organismen gefunden, die in hohem Grade für eine solche Pilzkrankheit verdächtig waren.

Multiple mediastinale Biopsien von den zwei anderen Patienten waren diagnostisch nicht überzeugend insofern, als keine Lymphknoten zu finden waren, die einen so frühen kollagenen Ersatz von nekrotischen Herden aufwiesen, obgleich das typische hyalinisierte fibröse und verkalkte Gewebe in grosser Menge vorhanden war.

Hauptpunkte einer Diskussion werden dargestellt, die anstelle der früheren Auffassung treten, wonach eine schwere chronische Mediastinitis und damit verknüpft ein Verschluss der oberen Hohlvene die Folge eines tuberkulösen Prozesses sei.

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Chemotherapy for Patients Following Dismissal from Tuberculosis Hospitals Throughout the United States

Results of a Survey of 424 Tuberculosis Hospitals*

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Policies and experiences related to the widespread practice of continuing chemotherapy for patients following their dismissal from tuberculosis hospitals could vary considerably from one institution to another and from one region of the country to another. Curiosity about the differences stimulated a survey of tuberculosis hospitals throughout the United States in 1956. This article presents an analysis of answers received from 424 hospitals with 84,346 beds for patients with tuberculosis.

Conduct of the Survey

It was anticipated that the response would be poor if the inquiries were numerous or if their answers required a search of clinical records and hospital files; hence a printed questionnaire consisting of a small series of questions was evolved. Most of these questions were followed by multiple-choice answers.

A mailing list of 519 institutions was made up from the Tuberculosis Hospital and Sanatorium Directory published in 1954 by the National Tuberculosis Association with corrections solicited from the office of the National Tuberculosis Association in New York City giving those hospitals that had opened, had closed or had been converted to other purposes since publication of the Directory. It was desired that the mailing list include all facilities listed for the care and treatment of tuberculosis within the United States, plus those that had opened since publication of the Directory, but excluding short-term diagnostic and surgical units, tuberculosis divisions of mental hospitals and units operated by the armed forces. These were eliminated because of the probability that the majority of their patients are not dismissed to their homes, but are transferred to other divisions of the same institution, or to other units within the same system or to other hospitals.

The questionnaires were mailed between June 6 and 22, 1956. Between August 15 and 21, 1956, a second questionnaire was sent to each institution that had failed to respond to the first mailing. By October 2, 1956, questionnaires had been returned from 424 hospitals. This represents an 81.7 per cent response to the survey based on the original mailing list of 519 hospitals meeting the afore-mentioned criteria for inclusion in the survey. The rate of return of questionnaires is presented in table 1.

*This survey was made possible in part by a grant from the Tuberculosis and Health Associations of the counties of Dakota, Freeborn, Goodhue, Mower, Olmsted, Rice, Steele, and Washington in the State of Minnesota. These counties comprise the district served by Mineral Springs Sanatorium.

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Regional distribution of the hospitals surveyed, their ownership or control, number of hospitals surveyed, their bed capacity and the percentage of response to the survey under each characteristic are given in table 2. The location of each of the 424 hospitals from which a questionnaire was returned is spotted on the accompanying map of the United States (see figure).

Results of the Survey

From this point on, the questions used in the questionnaire will constitute the headings for each topic to be discussed. Wherever applicable, responses to the questions will be organized in tables according to the multiple-choice answers provided in the questionnaire.

Do you require that the full course of chemotherapy be completed before you discharge your patients to their homes?

Answers to this question clearly divide the 424 hospitals into two groups: those that do and those that do not have a program of drug therapy extending beyond the period of hospitalization. Certain characteristics of each are compared in table 3. Patients are detained until their courses of chemotherapy are completed in 30 hospitals of all sizes; 10 of them are located in the South.

In what year did you inaugurate your program of chemotherapy at home for patients discharged from your institution?

The year of inauguration of a program of chemotherapy for patients following dismissal was given for 349 hospitals and is shown in table 4. A program was started as early as 1946 in four hospitals. By the end of 1951, patients were being dismissed from 59 hospitals with advice to continue treatment with drugs. The greatest development occurred during

TABLE I

RATE OF MAILING QUESTIONNAIRES AND RATE OF THEIR RETURN FROM TUBERCULOSIS HOSPITALS THROUGHOUT THE UNITED STATES*

	Week of Survey																	No Date	Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17		
First mailing of questionnaires	235	186	84				13	1											519
Questionnaires returned	4	88	130	71	38	19	7	6	6	2		1						4	376
Second mailing of questionnaires											138			1	1				140
Questionnaires returned											4	21	14	5	2		2		48
Questionnaires not returned																			95†

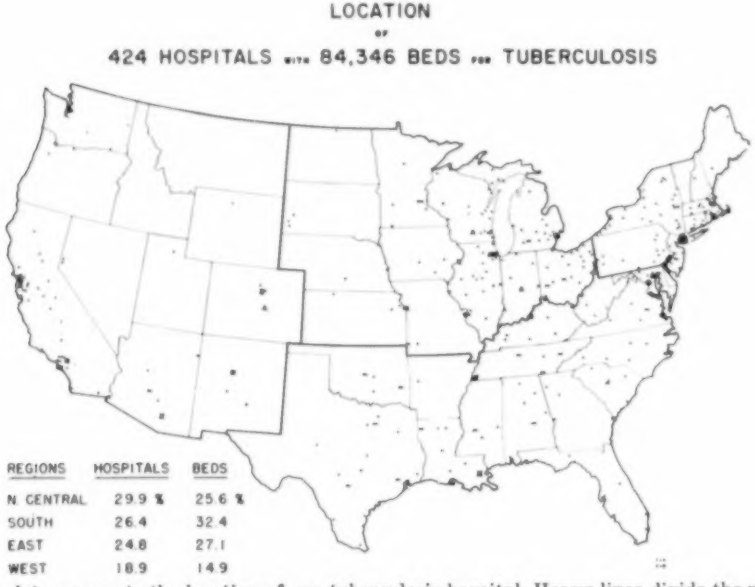
*The first week of the survey began on June 6, 1956. A questionnaire was mailed for the second time to all institutions from which no questionnaire was received after the first mailing. The survey was closed, arbitrarily, at the end of the seventeenth week, October 2, 1956.

†Inclusive of four returned questionnaires with inadequate or uninterpretable answers. These questionnaires are excluded from calculation of the percentage of questionnaires returned, referred to elsewhere.

TABLE II
CHARACTERISTICS OF TUBERCULOSIS HOSPITALS SURVEYED BY QUESTIONNAIRE IN THE UNITED STATES

Characteristics	Total Surveyed By Questionnaire	Questionnaire Returned	Questionnaire Not Returned	Response, Per Cent
Number of hospitals	519	424	95	81.7
Location by region				
North Central	147	127	20	86.4
South	141	112	29	79.4
East	124	105	19	84.7
West	107	80	27	74.8
Ownership or control				
Federal*	73	61	12	83.6
State	109	95	14	87.2
County	215	177†	38‡	82.3
City	31	26	5	83.9
Private	43	26	17	60.5
Semiprivate	48	39	9	81.3
Bed capacity				
Less than 100	225	160	65	71.1
100 to 299	201	180	21	89.6
300 to 499	54	48	6	88.9
500 or more	39	36	3	92.3
Number of beds	96,601	84,346	12,255	87.3

*Hospitals operated by the Federal Government include 53 Veterans Administration hospitals, seven hospitals for Indians and one general hospital.
†Includes 10 city-county hospitals.
‡Includes two city-county hospitals.



Each dot represents the location of one tuberculosis hospital. Heavy lines divide the map into the four regions defined by the Bureau of the Census.

the ensuing three years (1952, 1953 and 1954) when programs were instituted in 251 hospitals.

Programs were slowest to start in the North Central part of the country where no program for dismissed patients was inaugurated until 1949. As though to make up for lost time, programs were initiated in 35 hospitals in that area in 1952, the largest number to be started in any of the four regions in any one year.

TABLE III
ATTITUDE TOWARD CONTINUATION OF CHEMOTHERAPY FOR PATIENTS AFTER DISMISSAL FROM TUBERCULOSIS HOSPITALS

Attitude	Total Hospitals	Bed Capacity				Regional Location			
		Less Than 100	100 to 299	300 to 499	500 or more	North Central	South	East	West
Chemotherapy must be completed before dismissal of patients to their homes	30	12	10	4	4	4	10	8	8
Chemotherapy continued after dismissal of patients to their homes	394	148	170	44	32	123	102	97	72
Total Hospitals	424	160	180	48	36	127	112	105	80

TABLE IV
YEAR OF INAUGURATION OF PROGRAM OF CHEMOTHERAPY FOR PATIENTS AFTER DISMISSAL FROM TUBERCULOSIS HOSPITALS

Year Of Inauguration	Total Hospitals	Bed Capacity				Regional Location			
		Less Than 100	100 to 299	300 to 499	500 or More	North Central	South	East	West
1946	4	4	0	0	0	0	1	1	2
1947	4	3	0	1	0	0	2	2	0
1948	7	4	3	0	0	0	2	2	3
1949	3	1	1	0	1	1	1	1	0
1950	22	6	9	4	3	4	10	5	3
1951	19	5	9	2	3	8	6	1	4
1952	87	26	42	10	9	35	19	18	15
1953	89	31	41	10	7	30	12	29	18
1954	75	36	32	5	2	23	21	22	9
1955	33	13	13	3	4	9	11	3	10
1956	6	1	4	1	0	0	2	2	2
No answer given	45	18	16	8	3	13	15	11	6
Total hospitals	394	148	170	44	32	123	102	97	72

Approximately what percentage of your patients do you discharge with advice to continue chemotherapy at home?

Those answering questionnaires for a clear majority of hospitals (60.7 per cent) estimate that 75 to 100 per cent of their patients are advised to continue treatment with drugs after dismissal (table 5). While this advice is offered to more than three quarters of the patients dismissed from 73.6 per cent of the hospitals in the West, it is offered to more than three quarters of the patients being dismissed from only 46.4 per cent of the hospitals in the East.

What do you regard as the least amount of chemotherapy advisable for the average patient under your care? (Includes chemotherapy in sanatorium and after discharge.)

Twelve or more months of chemotherapy is regarded as the least amount advisable for the average patient in 90.4 per cent of all hospitals (table 6). Less than 12 months of chemotherapy is accepted as the minimal duration in 6.9 per cent of hospitals.

Although we anticipated trouble with interpretation of the phrase "average patient," qualified answers to the question were received from only nine hospitals. For the most part, these specified adjustment of the length of drug therapy to the type of case; for example, 12 to 18 months for patients with minimal tuberculosis and 18 to 24 months for patients with more extensive disease. The question was left unanswered in the returns from only two hospitals.

The large hospitals seem to favor longer courses of chemotherapy. Courses of 18 months or longer are advised in 61.8 per cent of the hospitals with 300 or more beds. The smaller hospitals are more equally divided on the question of duration. Courses of 18 months or longer are advised in only 46.5 per cent of the hospitals with fewer than 300 beds. Whereas 18 months is considered the minimal advisable course of drug therapy for the average patient in only 39.1 per cent of the hospitals in the East,

TABLE V
PERCENTAGE OF PATIENTS DISMISSED FROM TUBERCULOSIS HOSPITALS WITH ADVICE TO CONTINUE CHEMOTHERAPY AT HOME

Percentage of Patients Dismissed with Advice to Continue Chemotherapy at Home	Total Hospitals	Bed Capacity				Regional Location			
		Less Than 100	100 to 299	300 to 499	500 or More	North Central	South	East	West
Less than 25	41	15	19	5	2	6	10	18	7
25-50	51	15	26	4	6	12	18	14	7
50-75	61	21	27	4	9	24	13	19	5
75-100	239	97	97	30	15	81	60	45	53
Qualified answer	0	0	0	0	0	0	0	0	0
No answer given	2	0	1	1	0	0	1	1	0
Total hospitals	394	148	170	44	32	123	102	97	72

treatment of 18 months or longer is preferred in more than half of the hospitals in the rest of the country.

If one matches the duration of chemotherapy against the percentage of patients dismissed with advice to continue drug treatment at home, there appears to be a tendency to dismiss fewer patients with advice to continue chemotherapy from those hospitals where shorter courses of drug therapy are employed (table 7). This seems reasonable. Where courses of chemotherapy are shorter, there would be an opportunity for more courses to be completed before the patients are dismissed.

TABLE VI
LEAST AMOUNT OF CHEMOTHERAPY CONSIDERED ADVISABLE FOR THE AVERAGE PATIENT

Amount of Chemotherapy, Duration in Months	Total Hospitals	Bed Capacity				Regional Location			
		Less Than 100	100 to 299	300 to 499	500 or More	North Central	South	East	West
Less than 6	1	1	0	0	0	1	0	0	0
6-12	26	10	12	2	2	11	3	7	5
12-18	161	68	70	14	9	43	42	51	25
18-24	145	52	62	21	10	47	43	30	25
24-36	49	14	20	5	10	16	10	7	16
36 or more	1	0	0	1	0	0	0	1	0
Qualified answer	9	3	4	1	1	4	3	1	1
No answer given	2	0	2	0	0	1	1	0	0
Total hospitals	394	148	170	44	32	123	102	97	72

TABLE VII
CORRELATION OF MINIMAL DURATION OF CHEMOTHERAPY WITH PERCENTAGE OF PATIENTS DISMISSED WITH ADVICE TO CONTINUE CHEMOTHERAPY AT HOME

Minimal Duration of Chemotherapy, Months	Total Hospitals	Percentage Advised to Continue Chemotherapy at Home				
		Under 25	25-50	50-75	75-100	No Answer
Less than 6	1	0	0	1	0	0
6-12	26	5	5	5	11	0
12-18	161	23	19	37	82	0
18-24	145	9	21	12	102	1
24-36	49	3	5	2	38	1
36 or more	1	0	0	0	1	0
Qualified answer	9	1	1	3	4	0
No answer given	2	0	0	1	1	0
Total hospitals	394	41	51	61	239	2

Which drug or combination of drugs do you advise for the majority of patients going home on chemotherapy?

Isoniazid (INH) is a part of the regimens prescribed for patients being dismissed from 75.9 per cent of the hospitals (table 8). The most favored regimen is a combination of INH and one of the para-aminosalicylates (PAS). Isoniazid and PAS are prescribed for the majority of patients being dismissed from 56.3 per cent of the hospitals. This is no surprise considering the high therapeutic efficacy, low cost and minimal toxicity of INH. On the other hand, streptomycin, dihydrostreptomycin and streptoduocin are a part of the regimens prescribed in only 19.5 per cent of the hospitals. In no instance are streptomycin drugs (SM) or PAS being prescribed as sole medications; that is, combined with no other antituberculosis agent.

Fifty-six hospitals (14.2 per cent) submitted qualified answers. In almost all instances, the respondent designated two or three combinations of drugs without indicating the combination preferred for the majority of patients being dismissed to continue drug therapy at home. The selections are summarized in order of frequency in table 9. The most favored choices in 37 hospitals were INH-PAS, SM-INH and SM-PAS. The combinations listed in the survey questionnaire returned from one hospital included cycloserine. It seems unlikely that cycloserine would be prescribed for any appreciable number of patients who are to continue chemotherapy at home. The respondent for this hospital probably misunderstood the question.

TABLE VIII
REGIMENS ADVISED FOR THE MAJORITY OF PATIENTS BEING DISMISSED TO CONTINUE CHEMOTHERAPY AT HOME

Regimens Advised for Majority of Patients*	Total Hospitals	Bed Capacity				Regional Location			
		Less Than 100	100 to 299	300 to 499	500 or More	North Central	South	East	West
SM alone	0	0	0	0	0	0	0	0	0
PAS alone	0	0	0	0	0	0	0	0	0
INH alone	20	8	6	2	4	7	6	1	6
SM-PAS	20	10	6	2	2	4	3	9	4
SM-INH	41	17	18	4	2	18	9	6	8
INH PAS	222	82	98	21	21	73	64	50	35
SM-PAS-INH	16	4	8	3	1	4	2	5	5
Other regimens	18	7	7	4	0	3	4	7	4
Qualified answer†	56	19	27	8	2	14	14	18	10
No answer given	1	1	0	0	0	0	0	1	0
Total hospitals	394	148	170	44	32	123	102	97	72

*For abbreviations see text.
†See table IX.

Do you limit the majority of your patients to oral medications when they are discharged to continue chemotherapy at home?

Because of the discomfort, inconvenience and expense related to the administration of injectable drugs, it seemed likely that patients dismissed from the greater number of hospitals would be limited to oral administration of drugs. Such is not the case. Replies from only 50.0 per cent of the hospitals state that the majority of their patients are limited to oral use of drugs upon dismissal (table 10). The attitude on this question is about the same in hospitals of all sizes as well as in hospitals located in the West and in the North Central region of the country. The majority of patients dismissed from 62.7 per cent of the hospitals in the South and from only 37.1 per cent of the hospitals in the East are limited to oral medications. Whereas streptomycin is a part of the combinations prescribed for patients dismissed from only 13.7 per cent of the hospitals in the South, it is prescribed in more than 20 per cent of the hospitals in the rest of the country; this is true whether the three remaining regions are considered individually or as a whole. One wonders whether the controlling influence of having patients report to a physician's office, public health center or outpatient department for injections of streptomycin may not motivate the decision to use injectable drugs in certain parts of the country.

The use of public health nurses, public health centers, sanatoria or their outpatient departments for administration of streptomycin further emphasizes this disparity (see below). In the East, 67.0 per cent of the hospitals reported that the majority of their patients received their injections of streptomycin from these agencies, while in the South this applied to only 49.0 per cent of the hospitals.

TABLE IX
COMBINATIONS DESIGNATED BY THE RESPONDENTS FOR 56 HOSPITALS WITHOUT INDICATING A PREFERENCE OF REGIMEN FOR THE MAJORITY OF PATIENTS DISMISSED WITH ADVICE TO CONTINUE CHEMOTHERAPY AT HOME

Combinations designated	Hospitals
INH-PAS and SM-INH	13
INH-PAS and SM-PAS	12
INH-PAS and SM-INH and SM-PAS	12
INH-PAS and INH alone	6
All combinations designated	5
SM-INH and SM-PAS	2
INH-PAS and SM-INH and INH alone	1
SM-INH and SM-PAS-INH	1
SM-INH and INH alone	1
INH-PAS and SM-INH and cycloserine	1
INH-PAS and SM-INH and SM-PAS and SM-PAS-INH	1
"Prescription must be individualized"	1
Total hospitals	56

TABLE X

LIMITATION OF THE MAJORITY OF PATIENTS TO ORAL MEDICATIONS UPON DISMISSAL TO CONTINUE CHEMOTHERAPY AT HOME

Route of Medication	Total Hospitals	Bed Capacity				Regional Location			
		Less Than 100	100 to 299	300 to 499	500 or More	North Central	South	East	West
Limited to oral route	197	73	85	22	17	62	64	36	35
Not limited to oral route	194	75	83	22	14	61	36	60	37
Qualified answer	0	0	0	0	0	0	0	0	0
No answer given	3	0	2	0	1	0	2	1	0
Total hospitals	394	148	170	44	32	123	102	97	72

TABLE XI

MEANS BY WHICH THE MAJORITY OF PATIENTS RECEIVE INJECTIONS OF STREPTOMYCIN AFTER DISMISSAL

Person or Agency Administering Streptomycin Injections	Total Hospitals	Bed Capacity				Regional Location			
		Less Than 100	100 to 299	300 to 499	500 or More	North Central	South	East	West
Private physician	35	20	8	5	2	17	8	5	5
Public health nurse	93	27	48	7	11	20	31	30	12
Public health center	52	9	26	11	6	10	15	16	11
Sanatorium or outpatient department	83	34	36	7	6	44	4	19	16
Patient or family	30	16	12	1	1	6	10	6	8
Injection unnecessary	21	13	6	1	1	7	7	0	7
Other	8	2	4	2	0	3	1	3	1
Qualified answer	70	26	30	10	4	16	25	18	11
No answer given	2	1	0	0	1	0	1	0	1
Total hospitals	394	148	170	44	32	123	102	97	72

How do the majority of your patients get their streptomycin injections after discharge?

Answers from 57.9 per cent of the hospitals indicate that the majority of their patients obtain their injections of streptomycin by making use of agencies and services supported by public funds: public health centers, public health nurses, and sanatoria or their outpatient departments (table 11). Each area has its most favored method. The public health nurse is called upon to give injections to the majority of patients receiving streptomycin from 30 per cent of the hospitals in the East and South. The majority of patients receiving streptomycin report to the institutions or their outpatient departments in the case of 22.2 per cent of the hospitals in the West and 35.8 per cent of the hospitals in the North Central region of the country. Of any area, the private physician figures most prominently in the North Central region and least so in the East. The practice of training the patient or a member of his family to administer injections is, among the four areas, most prevalent in the West and least so in the North Central region.

The replies from 70 hospitals (17.8 per cent) were qualified, usually by designating two or more ways the patients received their injections of streptomycin, without indicating the most frequently employed method. In order of frequency the following were designated: public health nurse, public health center, personal physician, the sanatorium or its outpatient department and the patient or a member of his family.

The respondents for 21 hospitals (5.3 per cent) stated that injections of streptomycin were unnecessary because their patients were restricted to oral medications when dismissed to continue chemotherapy at home. None of these hospitals are situated in the East but are distributed equally among the three remaining areas of the country. Only two of them have more than 300 beds.

In most instances, who pays for the drugs used after discharge?

Drugs are supplied without charge to the majority of patients who continue chemotherapy after dismissal (table 12). Replies from 34.3 per cent of the hospitals indicate that the hospitals or their outpatient departments issue drugs free of charge. In the case of 31.2 per cent of the hospitals, the drugs are paid for by welfare or other public agencies. In 23.6 per cent, the patient pays for his own drugs, but he is least likely to do so in the West.

Qualified answers were submitted from 38 hospitals. These also reflected preponderant use of public funds to pay for drugs used following dismissal of patients.

Do your patients who receive chemotherapy at home obtain their drugs from your institution or outpatient department?

In a substantial majority of instances (55.3 per cent), patients obtain their drugs from the hospital or its outpatient department and do so most frequently in the North Central part of the country (table 13). Drugs are issued to patients dismissed from hospitals with less than 100 beds more frequently than is the case with patients dismissed from larger hospitals. Whereas drugs are issued from 58.2 per cent of the publicly owned institutions, they are issued from only 39.0 per cent of the privately owned hospitals.

Can your patients who leave against advice obtain drugs from your institution or outpatient department?

In the main, patients who leave against medical advice cannot obtain their drugs from the hospital or its outpatient department (table 14). In 60.2 per cent of the hospitals, drugs are not issued to patients who leave prematurely. A little more than half of the qualified replies from 39 hospitals indicated that drugs would be issued if the patients left without medical approval, but these replies included a variety of reservations and exceptions.

Are you aware of any significant number of patients failing to complete their course of chemotherapy at home as prescribed by you?

No definition of the phrase "significant number" was given in the questionnaire. Interpretation was left to the person answering. Obviously what constituted a significant number to one might not be considered so by another. Contrary to expectation, only one respondent submitted a qualified answer. The question was left unanswered in the case of nine hospitals. Replies indicated that a significant number of patients fail to complete the prescribed course of chemotherapy at home in the case of 15.5 per cent of the hospitals (table 15). Failures are greatest in the South and least in the East. Failures are no greater among patients from hospitals with less than 100 beds than among larger institutions; however, the fewest failures are among patients dismissed from the largest hospitals, 500 beds or more.

Failures are not much greater among hospitals where patients are limited to oral administration of drugs after dismissal (17.3 per cent)

TABLE XII
SOURCE OF PAYMENT IN MOST INSTANCES FOR DRUGS USED AFTER DISMISSAL

Source of Payment	Total Hospitals	Bed Capacity				Regional Location			
		Less Than 100	100 to 299	300 to 499	500 or More	North Central	South	East	West
Patient pays for own drugs	93	45	40	4	4	31	24	26	12
Sanatorium or outpatient department supplies drugs free of charge	135	52	58	15	10	59	14	35	27
Drugs paid for by welfare or other public agency	123	34	53	22	14	23	47	29	24
Other	4	3	1	0	0	2	2	0	0
Qualified answer	38	14	18	3	3	8	14	7	9
No answer given	1	0	0	0	1	0	1	0	0
Total hospitals	394	148	170	44	32	123	102	97	72

than they are among hospitals without such limitation (13.4 per cent). Failures are not significantly greater among hospitals where the majority of patients pay for the drugs they use after discharge (16.1 per cent) than they are among hospitals where public funds are employed to pay for the drugs used by the majority of patients after dismissal (14.3 per cent).

The respondents for several hospitals added a line of comment. Among those who thought that a significant number of patients failed to complete the prescribed course of drug therapy, one estimated his failures at 5 per cent, two estimated them at about 10 per cent, two at 20 per cent, one at 20 to 25 per cent and one said that his patients were issued one month's supply of drugs at a time, that at least 30 per cent of his patients did not appear for fresh supplies and that the urines of 40 per cent of the patients supposedly taking PAS showed a negative reaction when tested with 5.25 per cent solution of sodium hypochloride (clorox). On the other hand,

TABLE XIII
ACQUISITION OF DRUGS FROM HOSPITAL OR ITS OUTPATIENT DEPARTMENT

Patients Obtain Drugs From Hospital or Outpatient Department	Total Hospitals	Bed Capacity				Regional Location			
		Less Than 100	100 to 299	300 to 499	500 or More	North Central	South	East	West
Yes	218	92	94	19	13	88	45	44	41
No	156	52	67	21	16	35	46	47	28
Qualified answer	18	4	8	4	2	0	11	4	3
No answer given	2	0	1	0	1	0	0	2	0
Total hospitals	394	148	170	44	32	123	102	97	72

TABLE XIV
ACQUISITION OF DRUGS FROM SANATORIUM OR ITS OUTPATIENT DEPARTMENT BY PATIENTS WHO ARE DISMISSED AGAINST MEDICAL ADVICE

Patients Who Leave Against Medical Advice Can Obtain Drugs From Hospital or Its Outpatient Department	Total Hospitals	Bed Capacity				Regional Location			
		Less Than 100	100 to 299	300 to 499	500 or More	North Central	South	East	West
Yes	114	54	43	11	6	43	27	22	22
No	237	76	110	26	25	70	62	64	41
Qualified answer	39	16	15	7	1	8	11	11	9
No answer given	4	2	2	0	0	2	2	0	0
Total hospitals	394	148	170	44	32	123	102	97	72

among those who said they did not have a significant number of failures, five estimated the problem of failures at less than 10 per cent. From this small sample one might regard failures in excess of 10 per cent as significant and those numbering less than 10 per cent as not significant.

Under the protection of continued chemotherapy, do you discharge co-operative patients with cavitary tuberculosis whose sputum cultures have become consistently negative and for whom surgery is contraindicated or refused?

Co-operative patients with cavitary tuberculosis whose sputum cultures have become consistently negative and for whom surgical treatment is contraindicated or refused sometimes pose special problems. Under the protection of continued chemotherapy, patients of this kind are dismissed from 76.1 per cent of the hospitals (table 16). On the other hand, replies indicated that patients in this category are not dismissed from 18.0 per cent of the hospitals to continue chemotherapy at home.

TABLE XV
FAILURE OF A SIGNIFICANT NUMBER OF PATIENTS TO COMPLETE THE PRESCRIBED COURSE OF CHEMOTHERAPY AT HOME

Failure of Significant Number to Complete Prescribed Course of Chemotherapy At Home	Total Hospitals	Bed Capacity				Regional Location			
		Less Than 100	100 to 299	300 to 499	500 or More	North Central	South	East	West
Yes	61	23	27	8	3	15	25	10	11
No	323	122	138	35	28	107	74	82	60
Qualified answer	1	0	1	0	0	0	0	1	0
No answer given	9	3	4	1	1	1	3	4	1
Total hospitals	394	148	170	44	32	123	102	97	72

TABLE XVI
DISMISSAL OF CO-OPERATIVE PATIENTS WITH NONINFECTIOUS CAVITARY TUBERCULOSIS TO CONTINUE CHEMOTHERAPY AT HOME

Dismissal of Co-operative Patients with Noninfectious Cavitary Tuberculosis to Continue Chemotherapy at Home	Total Hospitals	Bed Capacity				Regional Location			
		Less Than 100	100 to 299	300 to 499	500 or More	North Central	South	East	West
Yes	300	98	134	40	28	84	82	79	55
No	71	38	28	2	3	31	11	11	15
Qualified answer	14	6	6	1	1	4	4	4	2
No answer given	9	6	2	1	0	4	2	3	0
Total hospitals	394	148	170	44	32	123	102	97	72

Comment

We have no way of defining how local or regional factors influence the policies and practices governing chemotherapy for patients after dismissal from the hospitals studied in this survey. The factors must be legion. Among them might be: unfortunate experiences in some hospitals, political interference, nature of ownership and control, distance from urban communities, proximity of medical centers, presence of major industries, development of public health programs, general economic status of patients, declination of hospital census, average length of stay in the hospital, cost of operation and many others. To identify them and to learn how they operate would have required a questionnaire composed of scores of questions.

We did encounter the unexpected. For instance, we did not think that a program of chemotherapy for patients following dismissal would have been inaugurated in many hospitals earlier than 1951. The concept of continuous chemotherapy for a year or longer was not widely accepted until 1951 or 1952. Yet 40 hospitals reported starting programs of drug therapy for dismissed patients prior to 1951, four of them as early as 1946.

It is interesting to us that less than 12 months of chemotherapy is accepted as the least amount of drug treatment advisable for the average patient in 27 hospitals. We are gratified to observe that the patient pays for his own drugs in most of the dismissals from 23.6 per cent of the hospitals. After evaluating our experience with patients who pay for their own medications—in our belief that a patient then has a palpable investment in his treatment, is less likely to throw his drugs away, is inclined to continue taking his medicine until the prescribed course is completed—it is surprising to observe that there is no significant difference in the percentage of failures among hospitals where the majority of patients pay for the drugs used after discharge than among the hospitals where public funds are employed to pay for those drugs.

Arguments can be marshalled for and against the matter of issuing drugs to patients who leave against advice. Some proponents say that one should make drugs available to patients who leave prematurely so that they will continue to receive correct combinations of drugs in appropriate dosage, to lessen the risk to the community, and so that, at least, contact will be maintained with the patient if only on an outpatient basis. The opponents contend that such a policy may increase the number of premature dismissals because patients will take advantage of the fact that they can leave without approval and yet continue to receive their drugs at home. One can, of course, show other reasons why drugs should or should not be issued to patients who leave against advice. Whatever the strength of the arguments, the fact is that the majority of hospitals form the opposition.

SUMMARY

In 1956 a questionnaire concerning the policies and practices relating to chemotherapy for dismissed patients was mailed to 519 tuberculosis hospitals in the United States and was returned from 424. In 30 (7.1 per cent) of the hospitals participating in the survey the full course of chemotherapy must be completed before patients are dismissed to their

homes. Among the remaining 394 hospitals (92.9 per cent) there is a program of drug treatment for patients following dismissal.

More than three quarters of the patients dismissed from 60.7 per cent of the hospitals are advised to continue drug therapy at home. A combination of isoniazid and one of the para-aminosalicylates is preferred in 56.3 per cent of the hospitals. Chemotherapy is prescribed for a total of 12 to 18 months (beginning during hospitalization) in 40.9 per cent of the hospitals. In the majority of instances drugs are not issued to patients leaving against medical advice. In most hospitals co-operative patients with noninfectious cavitary tuberculosis are dismissed to continue at home under the protection of antituberculosis agents.

Other data gathered by the survey are tabulated and reviewed.

RESUMEN

En 1956 se envió un cuestionario sobre le conducta seguida en quimioterapia para las altas en 519 hospitales de tuberculosos en los Estados Unidos y se recibió respuesta de 424 instituciones. En 30 (7.1 por ciento) de los hospitales que participaron en la investigación, todo el tratamiento médico debe estar terminado antes de que los enfermos salgan hacia sus hogares. Entre los restantes 394 hospitales (92.9 por ciento) hay un plan de tratamiento de los enfermos después de su salida.

Más de tres cuartos de los enfermos dados de alta de 60.7 por ciento de los hospitales son aconsejados que continúen el tratamiento en casa.

Una combinación de isoniacida y uno de los paraminosalicilatos se prefiere en 56.3 por ciento de los hospitales. La quimioterapia es prescrita por un total de 12 a 18 meses (empezando durante le hospitalización) en 40.9 por ciento de los hospitales. En la mayoría de los casos las drogas no son proporcionadas a los enfermos que salen contrariando el consejo médico. En la mayoría de los hospitales que tiene cavernas del tipo no bacilífero, si dan muestras de saber cooperar son dados de alta para continuar en su casa bajo la protección de las drogas antituberculosas.

Se presentan cuadros sobre otros datos reunidos así como su revisión.

RESUME

En 1956, un questionnaire concernant les règles et les moyens thérapeutiques en rapport avec la chimiothérapie pour les malades sortis de l'hôpital fut adressé à 519 hôpitaux tuberculeux dans les Etats-Unis, et fut renvoyé par 424. Sur 30 de ces hôpitaux (7,1%) participant au contrôle, le programme complet de chimiothérapie doit être terminé avant que les malades ne soient autorisés à retourner chez eux. Pour les 394 hôpitaux restants (92,9%) il existe un programme de traitement médicamenteux pour les malades après leur sortie de l'hôpital.

Plus des trois-quarts des malades autorisés à sortir dans 60,7% des hôpitaux sont priés de poursuivre le traitement médicamenteux à domicile. Une association d'isoniazide et d'un des para-aminosalicylates est préféreé dans 56,3% des hôpitaux. La chimiothérapie est prescrite pour un total de 12 à 18 mois (à partir de l'hospitalisation) dans 40,9% des hôpitaux. Dans la majorité des cas, les médications ne sont pas délivrées aux malades quittant l'hôpital sans y avoir été autorisés. Dans la plupart des hôpitaux, les malades coopératifs, atteints de tuberculose cavitaire

sans bacilles dans les crachats, sont renvoyés pour poursuivre chez eux la thérapeutique par les produits antituberculeux.

D'autres données recueillies par ce contrôle sont classées et analysées.

ZUSAMMENFASSUNG

Im Jahre 1956 wurde ein Fragebogen, die Richtlinien und Verfahren im Zusammenhang mit der Chemotherapie bei entlessenen Patienten betreffend, verschickt an 519 Tuberkulose-Anstalten in den USA und von 424 beantwortet. Bei 30 (7,1%) der an der Enquete beteligten Anstalten muss der ganze Turnus der Chemotherapie abgeschlossen sein, ehe die Patienten nachhause entlassen werden. bei den übrigen 394 Anstalten (92,9) besteht ein Programm der medikamentösen Therapie für Kranke anschliessend an die Entlassung.

Für mehr als ¾ der Pazienten, die von 60,7% der Anstalten entlassen werden, besteht die Anweisung, die Chemotherapie zuhasue weiter zu führen. Einer Kombination von INH mit einer der PAS-Präparate wird in 56,3% der Anstalten der Vorzug gegeben. Chemotherapie wird verordnet für insgesamt 12 to 18 Monate (mit Beginn während des stationären Aufenthaltes) in 40,9% der Anstalten. In der Mehrzahl der Fälle werden Heilmittel nicht ausgegeben an Kranke, die ihren Aufenthalt gegen ärztlichen Rat abbrechen. In den meisten Anstalten werden einsichtige Kranke mit nicht infektiöser kavernöser Tuberkulose entlassen, um zuhause kurgemäss weiter zu leben unter dem Schutz der antituberkulösen Arzneimittel.

Andere mit der Enquete gewonnene Daten werden tabellarisch weidergegeben und besprochen.

REFERENCE

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Pathogenesis of Bronchiectasis
An Experimental Study

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Of all the proposed theories, giving an explanation of the mechanism calling forth, and the persistency of bronchiectasis, none covers all the facts which have been observed in human pathology. Neither the hypothetical mechanical distension of a bronchial territory, recently presented by Croxatto and Lanary,[9] nor the deep lesions of the bronchial wall argued by Letulle, and more recently defended by Galy and Touraine[21] and mainly by Duprez,[19] are sufficient to explain at the same time "the acute and transitory dilatations," the etiological conditions under which they occur, the outbreaks of hypersecretion, the pulmonary and pleural lesions associated therewith, the circulatory perturbations constantly observed.

Taking into consideration the insufficiency of these theories, one of us,[11] in 1946, gathered a set of arguments in favor of a neurovasomotor theory, on the basis of anatomoclinical facts. All the facts published since then, and more particularly those concerning the circulatory perturbations,[16,19] have confirmed these first conclusions. However, to present as a theory that which an anatomopathological study had allowed to affirm, it seemed indispensable to us to look for an experimental confirmation.

The aim of this research is, therefore, to define the respective parts of localized endobronchial irritations, without stenosis, and that of circulatory perturbations and nervous alterations.

Experimental Conditions

If for all these experiments we have used dogs, this was not done for convenience's sake only. A triple advantage was to be gained: we knew its histology and its elementary lung lesions, since one of us had used it for previous studies.[12] Furthermore recent work had shown its endoscopic and radiological aspects.

We will not discuss all the techniques which were applied and the precautions which were taken to give us a maximum accuracy to these tests. Let it be enough if we say that the experiments which follow, were carried out with a maximum of care. All the operations were carried out under the same conditions as for a human patient, and particular care was given to anesthesia and postoperative nursing. During their survival, the animals were the object of thorough study and surveillance: clinical, radiological, endoscopic and at times when it was required by an experiment, angiocardiographical.

The same care was given to anatomical study. The injection of bronchial vessels has, in each case, been carried out by using the opaque mass

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developed by Mignot[28] and used by one of us in previous studies on the vascularization of pathological lung.[13-16]

Dissection and macroscopic study have always been carried out on an inflated lung, fixed following a technique developed by one of us, at Paul-Brousse Hospice.[11] After photography and radiography of the slices effected following the axis of the bronchi, we multiplied the samples. Lastly, to allow a correct study of the lesions, we carried out all the required colorations.

I — Endobronchial irritations, limited to a bronchial segment (main or lobar bronchus).

In order to determine if the bronchial stenosis represents the determining element, or if it is only, as is the bronchiectasis, the consequence of a localized bronchial irritation, we have applied three types of experiments, in order to determine a circumscribed bronchitis, without reducing the useful caliber of the bronchus.

— Anointment of the main bronchus, with a solution of KOH;

— Endobronchial irritation with a wire mesh apparatus;

— Association of the two processes.

a) *Anointment of bronchus with a solution at 20 per cent KOH*

Technique: On six dogs we have carried out, at eight days interval, under bronchoscopy, an anointment of the right main bronchus with a solution of KOH at 20 per cent. This application, carried out under general-pentothal-anesthesia, was limited to a cylindrical surface having a 1 cm. height, the upper limit of which was represented by the orifice of the main bronchus.

We took all necessary precautions to avoid both the aspiration of the caustic liquid and the appearance of an inflammatory stenosis. It is with this aim that we have carried out, on several occasions, during the days which followed the anointment, applications of adrenaline at 1 per cent. Antibiotics (penicillin and streptomycin) systematically used, enabled us to avoid postoperative complications.

Results: Two possible results were recorded:

1) For two dogs, despite adrenaline, a complete stenosis could not be avoided. Recorded after 15 days, it involved a characteristic clinical and radiological syndrome. Forty-five and 75 days after the first application we were able to record the following: While the main bronchus is completely obliterated by a sclerous diaphragm, the subjacent bronchi are normal, both macroscopically and histologically. We would however like to point out here that at the level of stenosis, the inflammatory processes remained localized to the endobronchus and never went beyond the fibro-cartilaginous blades.

2) In the other four cases, while the bronchus remained permeable, we observed bronchiectasis in subjacent territory.

These four dogs underwent a period of coughing which persisted until the last caustic application (4th), but the expectoration persisted during the whole length of their survival. Radiologically there was nothing abnormal.

FIGURE 1

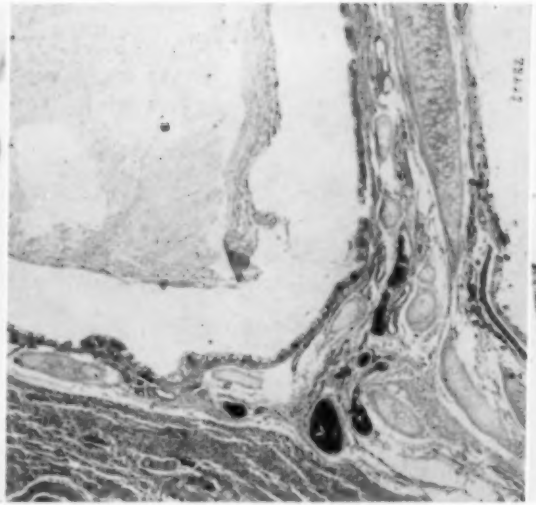

FIGURE 2

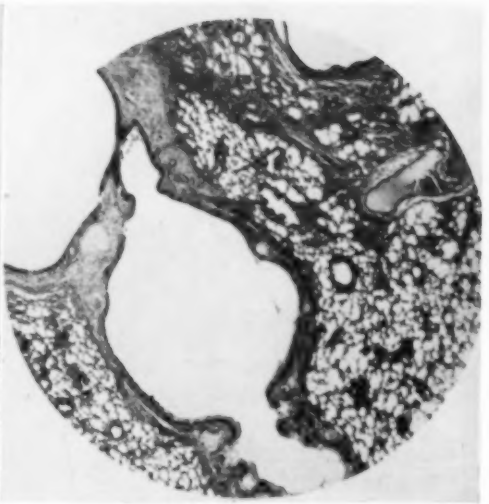

FIGURE 2B

Figure 1, Dog 39: Anointing of the right main bronchus with a solution at 20% KOH. Animal sacrificed 120 days after the experiment. Section of the right lower lobe, showing the importance of the dilatation at the level of cartilagenous bronchi.—*Figure 2, Dog 39:* Anointing of the right main bronchus with a solution at 20% KOH. Atrophic "bronchectasies" in a parenchymal in collapse. Animal sacrificed 120 days after the experiment. Hemateine eosine G x 20.—*Figure 2, Dog 32:* Anointing of the right main bronchus with a solution at 20% KOH. Dilatation of the small bronchi in a parenchyma in hypertrophic reticuled pneumonia. Animal sacrificed 120 days after the experiment. Hemateine eosine G x 40.

Whether they were sacrificed early (one month) or late (four months) the aspect was practically the same. The only difference residing in the depth of lesions.

In all cases, the opacification of arterial bronchial system carried out in accordance with a technique developed by one of us[14] has enabled us to ascertain a considerable development of bronchial circulation, but without anastomosis between the two arterial lung systems.

Macroscopically, the lung hilum is clustered with inflammatory ganglions. The main bronchus is shrunk but not obliterated. The bronchi, on the right side, under the affected segment were dilated. As far as the tributary parenchyma was concerned, it had in two cases the aspect of an atelectatic lung, and in two other cases it was normal.

Histologically, the shrinking of the main bronchus is cicatricial, being accompanied by a mutilation of all the wall elements and, very important fact, the inflammatory phenomena do not only concern the endobronchus, but also the peribronchus, where it is impossible to trace the nervous ganglionary relays. In the center of the sclerosis multiple vessels proliferate in all directions; a great number of which have the aspect and structure of the "Sperrarterien" of von Hayek, and of glomi.

The dilated subjacent bronchi have all the characteristics of human "bronchiectasis." The parenchyma which surrounds them is either in a state of collapse of or "hypertrophic reticuled pneumonia."

Nowhere have we come upon proof of an additional bronchial infection. The bronchi contained small quantities of mucus and none of them was either stenosed or obliterated.

b) *Endobronchial irritation with a metallic apparatus.*

Technique: In order to determine, by another means, a lasting endobronchial irritation, without the risk of provoking a stenosis of the

FIGURE 3, *Dog 64:* The section passing thru the axis of the two bronchi underlines the contrast between the two lobes. The bronchi are only dilated above the metallic apparatus. Animal sacrificed after 30 days.

lumen, we have made a small metallic apparatus which is introduced, through visual control under endoscopy, and is placed with the help of tracheal forceps in the segmentary bronchus previously chosen. It has its form and size: conical trunk composed of wire mesh, it never measures more than 2 cm. in height.

It was placed three times in the right main bronchus, twice in the lower right lobary and once in the lower left lobary.

As in the case of the previous experiments it was possible to avoid infectious complications, by using antibiotics.

Results: In all cases, after a period of cough lasting a few days, the foreign body was well tolerated, it has however always involved a bronchial hypersecretion, which was perfectly visible at the time when endoscopy controls were carried out and often resulted in a mucous expectoration.

1) For those animals which were sacrificed at an early stage (3, 15, or 20 days after the placing of the apparatus) there is no bronchial dilatation in the subjacent territories. Inflammatory phenomena were limited, at the place of the metallic cylinder, to the endobronchus.

2) On the contrary, after 60, 90 and 150 days, we were able to ascertain in each case important bronchiectasis.

At the location of the metallic apparatus, all the levels of the bronchial wall participate in the inflammatory phenomena, the endobronchus, as well as the peribronchus. At its level the same modification as when using KOH are to be found: sclerosis, development of bronchial circulation, nervous alterations.

Bronchectasies resides exclusively in the territory of the irritated bron-

FIGURE 4

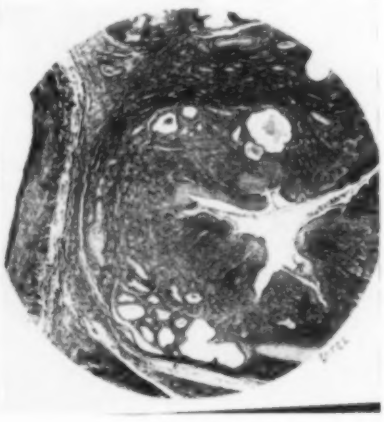

FIGURE 5

Figure 4, Dog 64: Atrophic "bronchiectasis" in an almost normal pulmonary parenchyme. On this preparation is to be noted the apparition of peribronchial sclerosis. Animal sacrificed on the 30th day. Reticuline—Masson-trichrome (G. x 30).—*Figure 5, Dog 68:* Endobronchial irritation with the metallic apparatus. Hypertrophic bronchiectasis with sclerosed wall. Dog sacrificed 100 days after the experiment. Vilder (G. x 30).

chus, and have the morphology, and the structure, of chronical inflammatory bronchiectasis (90 days) or sclerosed (150 days).

As can be seen from the arteriographic plates and the histological preparations, this experiment differs from the preceding ones, due to the importance of circulatory perturbations and, parallel to this, the alterations of the bronchial wall and of the tributary parenchyma which is, almost everywhere, in a state of "hypertrophic reticuled pneumonia."

c) *Irritation of the main bronchus, by joint anointment of the bronchus with a solution of KOH and placing of a metallic apparatus.*

Technique: During the same operating time, first an anointment with a solution of KOH is carried out, then a previously prepared metallic cage is immediately placed in the irritated zone.

Results: Of the four dogs which underwent this double aggression, two survived, and were sacrificed one and four months later. The facts ascertained here only differed from those previously noted thru the intensity of changes.

The development of the bronchial circulation attained a considerable intensity, and in various points anastomosis between the two arterial lung systems were to be found. The ganglions of the lung hilum were very big. While remaining permeable, the main bronchus was the site of so much inflammatory changes that it was difficult, at this level, to find evidence of the initial structure.

All the normal elements have disappeared, to make room for a sclerosis which goes very far into the peribronchus, destroying completely all the

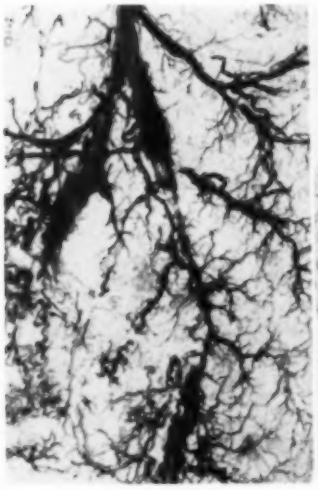

FIGURE 6

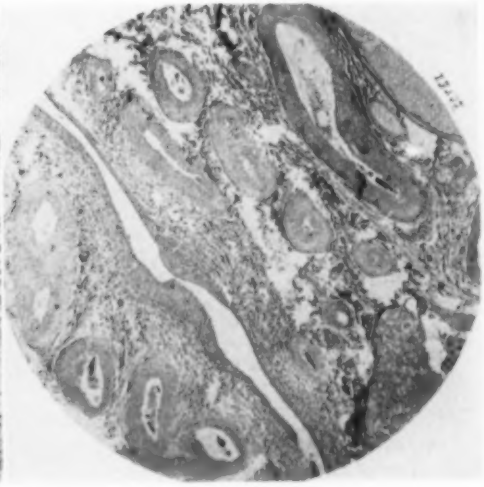

FIGURE 7

Figure 6, Dog 71: Endobronchial irritation with the metallic wiremesh apparatus. Development of the arterial bronchial network. X-ray of a slice after injection of the bronchial arteries (G. x 6). Dog sacrificed after 60 days.—*Figure 7, Dog 1:* Ligature of the left pulmonary artery. Development of checking segments and of bronchial arteries in the bronchial adventice of the cartilagenous bronchi. Masson trichrome—Reticuline (G. x 40).

ganglionary nervous relays. The bronchi situated in the tributary territory are dilated and present morphological characteristics of chronic "bronchectasies," with thick and inflamed walls. The parenchyma, grooved with collagene sclerosis strips, is the site of a hypertrophic reticuled pneumonia, at the dystrophic stage.

It is possible to draw several conclusions from these three groups of experiments.

It is easy to ascertain that when the stenosis exists, it is witness of a bronchial irritation, since it is in those cases when the arial passage has remained permeable, and in those cases only, that bronchiectasis have developed in the tributary territory. Two other facts are associated with this, which are of great importance for discussion. Infection plays no part and in addition, a fact which we wish to underline, it is not at the level of irritation that the distension took place, but in the territory situated above.

The analysis of the protocols, briefly resumed above, allows us to state a few positive facts concerning the mechanism of dilatation.

We have noted that it took place only when the bronchial adventice participated in the inflammatory phenomena, and more particularly so, when the ganglionary relays had been altered or had completely disappeared. This enables us to think that there is a strong relation between the nervous alteration of irritated segment and the distension of the bronchus situated above.

Furthermore, the differences which separate the atrophic "bronchectasies" obtained thru the application of KOH and the hypertrophic forms resulting from the irritation with a metallic apparatus, are linked with more or less important circulatory perturbations. These facts allow us, to think that the determination of "bronchectasies" depends upon the bronchial adventia and its associated nervous and vascular elements, and not from the reduction of the bronchial caliber and the stasis of secretion products.

This point stated, it remained to define the respective parts of the circulatory disturbances and the nervous alterations.

A—*Circulatory disturbance*

We had to determine if the circulatory disturbance which had been observed, both in the human clinic and in the preceding experiments, had to be considered as a corollary of parietal lesions, or as a determining element. In an endeavor to answer this double question we carried out two types of experiments: the first aimed at a brutal modification of the pulmonary hemodynamics, the others reproduced as closely as possible the circulatory syndromes observed in human "bronchectasies."[1, 10]

I—*Structure of a lung submitted to an exclusively "systemic" circulation.*

Owing to their differences the Blalock and Potts anastomosis have allowed the analysis of the repercussions which are involved for the bronchus and the parenchyma, thru the circulation in the pulmonary artery of blood richer in oxygen than is normal. We have carried out each type

of anastomosis on three dogs and were thus able to compare the structural modifications which they entrained, after 20, 30 and 50 days.

The physiopathological difference has its anatomic corollary. In both cases the bronchi preserve their normal structure but the same is not true for the parenchyma. Whilst the Blalock anastomosis does not involve any modifications, the alveolary system of the lungs of the dogs which had Potts anastomosis constantly changed. The lesions are characterized by an "hypertrophic reticuled pneumonia," diffused to the whole of the left pulmonary parenchyma. To this is associated a sclerosis of the interlobular partitions.

It seems interesting to us to link the physiopathological syndrome and the anatomic lesions observed, with what is to be found in the case of an unilateral absence of a branch of the pulmonary artery trunk.

In both cases the bronchial structure remains normal, while the parenchyma always presents a diffused thickening of the interalveolary partition. The strong parallelism between the physiopathological syndrome and the anatomic lesions shows that the alterations of the alveolary system of the lung are in close relation with circulatory perturbations.

The experiments which involve the development of the arterial bronchial system and the creation of anastomosis between the bronchial and the pulmonary arteries, a syndrome which is the result of the occlusion or of the reduction of the caliber of the pulmonary artery, are more instructive.

II—*Structure of the lung after ligature of the left pulmonary artery.*

Whatever the date of the observation may have been (100, 120, 180 days) we constantly noted an hypertrophy of the "systemic" vessels.

The development of this circulation does not only affect the bronchial arterial system, but also the pleuro-hilary network. It is thus that in all cases we observed the development of a circulation going from thoracic wall to lung, thru the membranous veils which linked the lung to the operational scar.

To this hypertrophy of the "systemic" vessels, the apparitio of anastomotic formation with the pulmonary artery, is constantly associated. They either take on the aspect of von Hayek's "Sperrarterien," or that of glomi, which were described by one of us for the first time in the pathological lung, with Paillas and Sors.[13] These anastomotic formations reside both in the bronchial adventice and in the adherential veils. They are more numerous and different, the later the dogs were sacrificed.

The thus created vascular syndrome, is accompanied only by very small modifications of the broncho-pulmonary structure: malpighian metaplasy of the large bronchi, sclerosis of the chorion and a discreet "hypertrophic reticuled pneumonia."

III—*Structure of the lung, after stenosis of the pulmonary artery.*

Technic: Thru a series of separate points staged along the inner edge of the left pulmonary artery, we easily arrived at a permanent reduction of its caliber, to one third of its normal size.

Results: Whether the constatations were made 50, 76, 80 or 90 days after the intervention, the stenosis of the pulmonary artery only had very

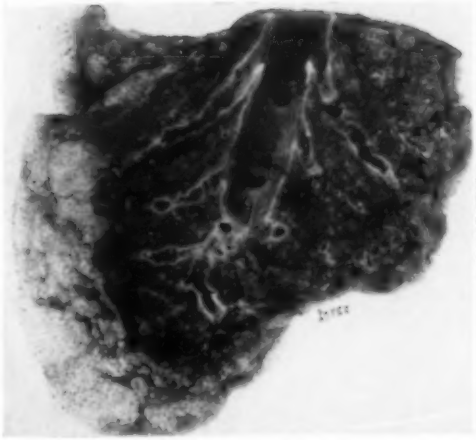

FIGURE 8

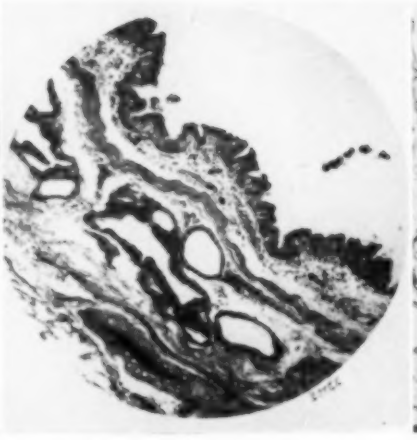

FIGURE 9

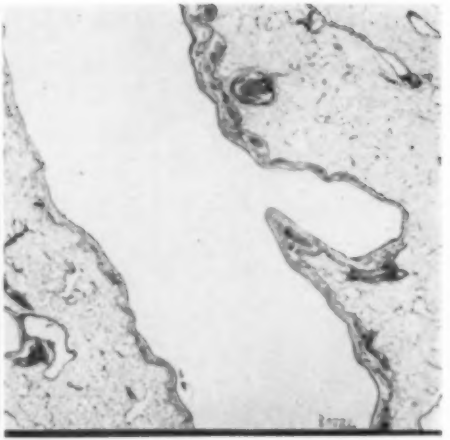

FIGURE 10

Figure 8, Dog 53: Bronchial distension after alcoholization of the right vagosympathic trunk. Animal sacrificed 180 days after the experiment.—*Figure 9, Dog 53:* Perpendicular section of the pulmonary hilum, showing the atrophy of the elements of the bronchial wall. Hemateine eosine (G. x 80).—*Figure 10: Dog 53:* Longitudinal section of distended bronchi. Atrophy of all the elements of the bronchial wall. Hemateine eosine (G. x 8).

small consequences, not very different, in fact, from those we had noted after the ligature of the pulmonary artery. We only wish to note that the hypertrophy of the bronchial arterial system, just as that of the pleuro-hilary network, remains less important and that the precapillary anastomosis only develop at a late stage.

These four types of experiments allow us to draw a few conclusions on the part played by circulatory perturbations in the modifications of the broncho-pulmonary structure.

It is certain that the circulatory perturbations which we caused in the dogs, only resulted in a few minor changes in the bronchial and the pulmonary structures. This does not, however, allow us to minimize the part played by the modifications of the circulatory rate of flow, since we were never able to produce an anatomical and physiopathological syndrome identical to that observed in human pathology. The fact that a slightly developed vascular syndrome is accompanied by notable modifications enables us to think and believe that more important perturbations would have had as a corollary more marked alterations of the broncho-pulmonary organism.

B—*Part played by nervous alterations*

During anatomic studies and in the preceding experiments, we were struck by the importance of alterations of the peribronchial nervous system. In order to determine the repercussions on the structure of the broncho-pulmonary organism which they involve, we carried out an alcoholization of the right vago sympathetic trunk in the cervical region.

Technic: Under general anesthesia, with pentothal, we carried out an incision along the posterior edge of the right sterno-cleido-mastoidian. After the section of the medium cervical aponevrosis, and the infiltration into the sheath of the vessels of novocaine at 1 per cent, we were able to isolate the vago-sympathetic trunk. A big injection of novocaine precedes by a few minutes the injection of absolute alcohol into the inside of the nervous trunk. This alcoholization is carried out 4½ cms. above the branches which are exchanged between the vago-sympathetic trunk and the stellate ganglion, i.e. approx. five fingers width, above the sternal manubrium. As soon as a blackish coloration becomes apparent, the nerve is carefully reintegrated into its place. The sheath of the vessels is closed with a 000 catgut, and the wall reconstituted on four levels.

Results: Operational sequels went off without incidents, owing to the systematic application of antibiotics, which enabled us to avoid infectious complications.

We feel that four particularly interesting facts should be underlined. During 10 days the dogs showed a right sided enophtalmy but without any other associated sign (cardiac, tensional). X-ray film did not show any transparency anomalies. The most interesting facts were however noted during endoscopic controls: the first 10 days were marked by hypersecretional phenomens, which disappeared progressively. At the end of 100 days, whilst the bronchial mucous presented an almost normal character, though drier, bronchial secretions had taken on an almost solid consistency,

and presented tapioca-like grains, accumulated near the segmentary orifices of the right lung. To these expectoration modifications were associated motricity and sensibility alterations of the bronchus. To inertia was added an almost complete disappearance of the cough provoking reflex.

Of the seven dogs which had been operated, four were retained for analysis of the results, the three others having presented breathing complications during the time of their survival ("metastrongyloïdose," canine influenza).

At autopsy, which was carried out after varying lengths of time (60, 120, 150 and 180 days after alcoholization) we did not observe any notable modifications. But the vascular injections, opacifying the bronchial arterial system, showed on the right side an exaggerated bronchial circulation, as well as a few anastomosis with the pulmonary artery. The dissection of the right lung revealed, in every case, a very important increase of the bronchial caliber, this being the larger the longer the dog had survived.

The histological aspect is monomorph, identical on all the samples taken and characterized by an atrophy of all the bronchial elements, and more particularly of the muscles, glands and cartilages. In the bronchial adventia, all nervous ganglionary structure had disappeared, and a multitude of small vessels belonging to the arterial bronchial system were to be found, as is ascertained thru the presence of the injected mass in their opening. The tributary parenchyma of the dilated bronchi is normal.

This experiment enables us to draw several conclusions as to the part played by nervous alterations.

The alcoholization of the right vago-sympathetic trunk, involving systematic alterations of the bronchi of the right lung, without any lesions of the opposed lung, allows us to confirm the conclusions of Kaunitz and Andersen[23]: contrary to what happens in man, the pneumogastric of the dog innerves exclusively the homolateral lung.

The disappearance of the nervous peribronchial ganglions cannot allow us to affirm that these relays belong to the pneumogastric since, as has been shown by Chase and Ranson[6] the sympathetic and parasympathetic fibres are entirely mixed in a common trunk, in the cervical region, location of our alcoholization.

Nevertheless we think that if, owing to this fact, it is impossible for us to define with precision the disturbance which we started, we may however establish a relation between the atrophy of the nervous ganglions and that of the elements of the bronchial wall. Consequently, the bronchial distension may be considered as a direct corollary of the atrophy of the peribronchial ganglionary nervous system. We thus arrive at conclusions very near to those of Staudacher, Girardi and Bertolini.[30] By effecting an ennervation of the peribronchus these authors were able to reproduce bronchial distensions similar in all points to those which we obtained by acting at a distance on the nervous trunks.

All these experiments confirm therefore that which an accurate anatomopathological study had allowed one of us to formulate in 1946[11]:

"Permanent bronchial ectasis results from the fixation of a functional distension and, more probably, from the persistency of the nervous irritation which produces it."

The main reasons are of a nervous neuro-vegetatif origin, as is shown both in action carried out at a distance on the nervous conductors, and by the local ennervation carried out by Staudacher.[30] Secondary reasons, able to involve parieto-bronchial and pulmonary alterations, which represent the substratum of what is agreed to call "bronchectasies," are however circulatory, as is pointed out by our first experiments. Since it is only when these perturbations were important ones that we observed parieto-bronchial changes, identical to those encountered in human pathology.

In reaching such conclusions, we check with two general physiopathological laws, at lung level. Functional disturbances precede the lesion which, itself, is only the expression of an alteration of the neuro-vegetatif system.

SUMMARY

On the basis of data supplied by anatomic, clinical and physiopathological study, on a large number of "bronchectasies," the authors have endeavored to determine, thru experimentation on dogs, the respective part of bronchial stenosis, circulatory modifications and nervous alterations in the genesis of bronchial dilatation.

A first group of experiments including several types of non stenosing endobronchial irritations, leads them to deny the part played by the stenosis and to consider "bronchectasies" as the consequence of circulatory perturbations and nervous alterations.

The two other groups of experiments serve to define the part played by each of these factors.

After analyzing the facts which were observed, it is possible to think that the nervous factors are intimately linked with the distension mechanism and that the parieto-bronchial and pulmonary changes are the result of circulatory perturbations.

RESUMEN

Sobre la base de los datos proporcionados por los estudios anatómico, clínico y fisiopatológico, en gran número de "bronquectasias" los autores han tratado de precisar por experimentos en perros, la parte que corresponde a la estenosis bronquial, a los cambios circulatorios y a las alteraciones nerviosas en la producción de la dilatación bronquial.

El primer grupo de experimentos incluyendo varias formas de irritación endobronquial no estenosante los condujo a negar el papel desempeñado por la estenosis y a considerar la "bronquiectasia" como consecuencia de trastornos circulatorios y nerviosos.

Los otros dos grupos de experimentos sirven para definir la parte desempeñada por cada uno de estos factores.

Después de analizar los hechos observados, es posible pensar que los factores nerviosos están íntimamente ligados con el mecanismo de la distensión mecánica y que los cambios parietobronquiales así como los pulmonares son el resultado de perturbaciones circulatorias.

RESUME

Partant des donnés fournies par l'étude anatomique, clinique et physiopathologique d'un grand nombre de bronchectasies, les auteurs ont cherché à préciser par l'expérimentation sur le Chien, la part respective de la sténose bronchique, des modifications circulatoires et des altérations nerveuses dans la genèse des dilatations bronchiques.

Un premier groupe d'expériences comprenant plusieurs types d'irritations endobronchiques non sténosantes les amène à nier le rôle joué par la sténose et à considérer les bronchectasies comme la conséquence de perturbations circulatoires et d'altérations nerveuses.

Les deux autres groupes d'expériences servent à définir le rôle joué par chacun de ces deux facteurs.

Après une analyse des faits observés et une discussion, il est possible de penser que les facteurs nerveux sont intimement liés au mécanisme de distension et que les remaniements pariéto-bronchiques et pulmonaires sont le fait des perturbations circulatoires.

ZUSAMMENFASSUNG

Auf der Basis von Erhebungen an einer grossen Zahl von "Bronchiektasen" und unterstützt durch anatomische, klinische und pathophysiologische Untersuchungen haben sich die Autoren bemüht, durch Versuche an Hunden den besonderen Anteil der Bronchialstenose, der Kreislaufveränderungen und der nervösen Störungen bei der Genese der Bronchialerweiterung zu bestimmen.

Eine erste Reihe von Experimenten einschl. verschiedener Typen von nicht stenosierenden bronchialen Reizzuständen war der Anlass für die Autoren, die Rolle, die die Stenose spielt, in Abrede zu stellen und die "Bronchiektasie" als die Folge von zirkulatorischen Störungen und nervösen Reizzuständen anzusehen.

Die beiden anderen Gruppen von Experimenten dienen der Bestimmung des Anteils, den jeder dieser Faktoren spielt.

Nach Auswertung der beobachteten Tatbestände ist der Gedanke möglich, dass die nervösen Faktoren eng verknüpft sind mit dem Mechanismus der Erweiterung und dass die Veränderungen der Bronchialwand und der Lunge das Ergebnis von Zirkulationsstörungen sind.

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BOOK REVIEWS

"DER LUNGENBOECK IM ROENTGENBILD," by K. Wurm, H. Reindell and L. Heilmeyer; Georg Thieme, Stuttgart, 1958, 220 pages, $18.55.

This is a prodigiously and beautifully illustrated monograph. In view of the increasing interest in its subject, sarcoidosis, it renders inestimable service by offering in one volume the variegated pulmonary manifestations of this disease.

The presentation is complete, thorough and highly competent. The vast personal experience of the authors is offered with sound critical evaluation which is bound to assist the reader in the daily clinical application of information gathered by the authors. The format of the book is good, the paper and technical production are excellent.

Andrew L. Banyai, M.D., F.C.C.P.

"INTRACARDIAC PHENOMENA IN RIGHT AND LEFT HEART CATHETERIZATION," by Aldo A. Luisada and Chi Kong Liu; Grune & Stratton, New York, 1958, $9.50. Pp. 175.

The first edition of this book published in 1956 under the title "*Cardiac Pressures and Pulses*" has been revised and extended to be all inclusive in its presentation of its subject *Intracardiac Phenomena*. Further techniques including left heart catheterization and intracardiac phonocardiograms and electrocardiograms have been added. The book is very detailed in its description of these procedures, and it is complete with diagrams and tables recording normal and abnormal findings. The cardiac physiologist could use it as a reference work and will probably find it worth while to follow some of the techniques described. However it does not appear to me that it is a book for the beginner in this field. The bibliography is grouped in the back without any reference to the text. It seems to us it would be more useful if it were indicated in the text where these references applied. I can highly recommend this book as fully covering the field of *Intracardiac Phenomena*.

Arthur E. Lamb, M.D., F.C.C.P.

An Epidemic of Histoplasmosis in a Family*

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Histoplasmosis is caused by the fungus *Histoplasma capsulatum*, which enters the body through the lungs is disseminated via the blood stream and involves chiefly the lungs and the reticuloendothelial system. It is usually a benign subclinical process, detectable only by the conversion of the skin test. In a moderate number of persons the primary infection is followed by dissemination which is manifested by a mild illness lasting several weeks. In this intermediate group the complement fixation test is usually positive, and the organisms can sometimes be identified microscopically in tissue, blood or sputum or by culture on appropriate media. The pulmonary lesion is in the form of a coarsely nodular infiltration which later calcifies. Other rarer manifestations of the disease are: a chronic disseminated process, tertiary cavitary lesions of lung resembling chronic pulmonary tuberculosis and a fulminating and highly fatal dissemination.

In central United States the organism is a common saprophyte in soil,[1] especially in the soil from an environment where chickens or other fowl have lived.[2] Human primary infection in this area, as reflected by positive skin test, varies from 27 to 73 per cent or more of the population.[3] When several persons are heavily exposed at the same time and become ill, a so-called epidemic results. The authors wish to report an epidemic which occurred in the six members of a family residing somewhat outside the endemic region of the Mississippi Valley from which most epidemics have previously been reported.

A family of migrant workers consisting of father, mother and four children ranging in age from five to 11 years had moved from Maryland to Virginia within the preceeding year and were living in a country farm house on the north branch of the Shenandoah River in Warren County, Virginia. On a hot dry Sunday, believed to have been May 13th, 1956, they decided to clean their chicken house. The father shoveled most of the guano from the floor while the children assisted him or simply entered and left the shack several times. The mother walked into the chicken house briefly on a single occasion. During this activity, the atmosphere was so filled with dust that they coughed frequently and on several occasions had to emerge for fresh air. On about May 23rd, 1956, the father became ill with fever and prostration. He was sufficiently ill to see a physician, who thought he had pneumonia. After 10 days at home he gradually improved. He continued to have weakness, however, pleuritic pain in the chest, a nonproductive cough and low grade fever. On June 8, 1956, he was admitted to the Veterans' Administration Hospital at Martinsburg, West Virginia, where he remained a month. This hospital has been good enough to make their findings available, as follows.

Physical examination revealed a man in his mid thirties who was well developed, but quite thin, with a languid and chronically ill appearance. The liver edge could be felt on deep inspiration. Questionably enlarged, non-tender, discrete, and movable cervical and inguinal lymph nodes were palpated.

The urinalysis was normal. The white blood cell count was 7000 with a normal differential count. The sedimentation rate was 47 mm./hour. A roentgenogram of the chest made several years earlier at the same institution had shown nothing abnormal (Fig. 1A). The roentgenogram made on his admission in June, 1956, however, revealed extensive granular infiltration, widely and uniformly distributed throughout both lungs. (Fig. 1B). The skin test with histoplasmin was reported as 4+ within 72 hours. The complement-fixation test was positive in a titer of 1:128. The blastomycin titer was 1:16, but the coccidioidin was negative. The patient continued to have an irritative cough, mild pleuritic pain and low-grade fever. After exactly one month he went home on leave and did not return.

*From the Division of Thoracic Surgery and the Department of Pediatrics of the University of Virginia Hospital.

TABLE I

COMPLEMENT-FIXATION TITERS WITH YEAST PHASE ANTIGEN OF HISTOPLASMA CAPSULATUM

Case No.	Patient	July 20, '56	Dec. 10, '56
1.	E. H.	1:128	
2.	T. H.	1:32	1:8
3.	C. H.	1:256	1:16
4.	J. H.	1:64	1:32
5.	E. W. H.	anti-complementary	1:8
6.	N. H.	Negative	Negative

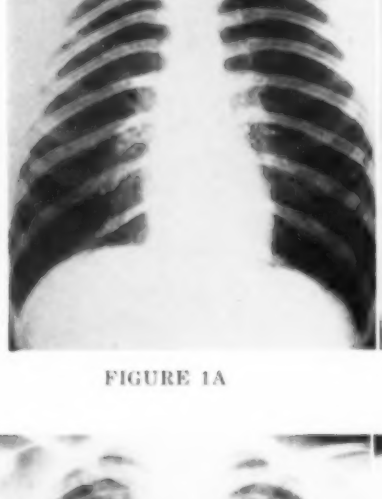

FIGURE 1A

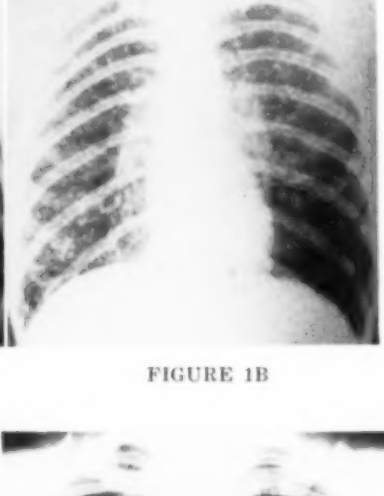

FIGURE 1B

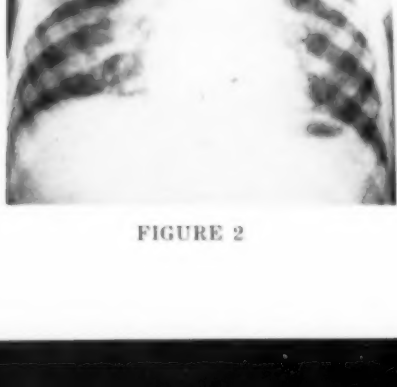

FIGURE 2

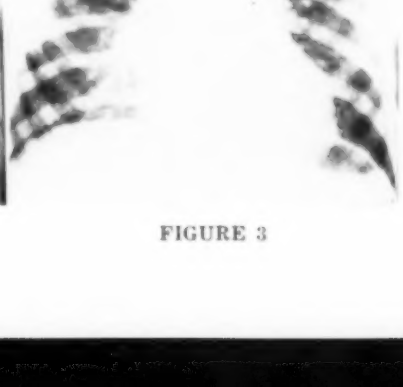

FIGURE 3

A day or so after onset of symptoms in the father, the children became feverish and irritable, with anorexia, nausea, malaise, frontal headache, and non-productive cough. Since the father had been hospitalized with a pulmonary infection of unknown etiology, roentgenograms of the four children were made by the local health department. All films showed pulmonary changes varying from spotty infiltration to multiple heavy nodules with miliary distribution (Fig. 2-5). It was possible to bring the children and the mother to the Pediatric Clinic of the University of Virginia Hospital for two visits, the first on July 20th, 1956, and the second on August second, 1956.

On examination the children were malnourished but alert. They all had minimal to moderate adenopathy in the cervical and inguinal regions, but neither spleen nor liver could be palpated. There were no other localizing signs and none had fever at this time.

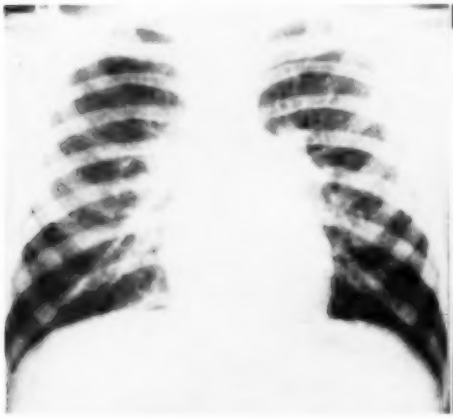

FIGURE 4

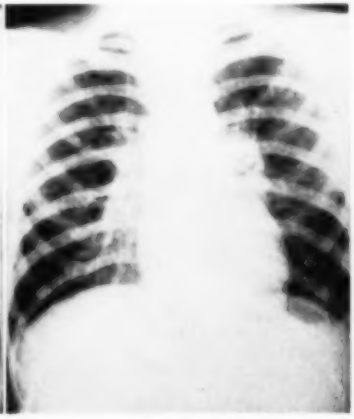

FIGURE 5

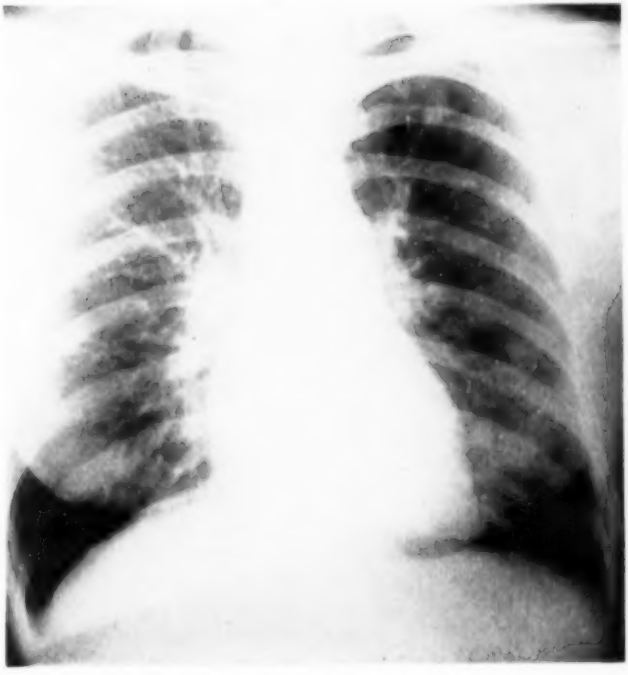

FIGURE 6

Urinalyses on the four children showed no abnormality. The white blood cell count and differential count on each child were within normal limits, as were the values for hemoglobin and the hematocrit. Intradermal histoplasmin tests on each child were interpreted by a physician between 48 and 72 hours after performance as representing 3+ reactions. In the same period a Mantoux test (Old Tuberculin 1:1000) was negative. The complement fixation data are summarized in Table I. Additional roentgenograms of the chest showed coarse, irregular, nodular to patchy soft densities scattered symmetrically through both lung fields with mild to moderate hilar adenopathy in all.

Approximately two weeks later the children returned to the Pediatric Clinic for a follow-up visit. Marrow was obtained from the iliac crest from each child and cultured on various appropriate media, but no growth was present at the end of eight weeks.

The mother was examined on each of the two visits to the Clinic. For several weeks prior to her first visit she had experienced malaise, anorexia, vague and fleeting chest pains, weakness, feverishness, cough productive of mucoid sputum and exertional dyspnea. Despite these manifestations of illness she had been able to care for the children while her husband was hospitalized. On physical examination she proved to be a 31-year-old white woman, an epileptic of moderate severity, whose attacks were controlled with sedatives and anti-convulsive medications. She was well developed and well nourished and presented no significant abnormal findings. The urinalysis and blood studies were within normal limits. A histoplasmin skin test, read at 72 hours, showed an area of erythema and induration approximately 3 cm. in diameter with vesiculation at its center, a result interpreted as 4+. The tuberculin (1:1000 O.T.) skin test was negative. The complement fixation test was negative. Roentgenograms of the chest revealed several localized areas of infiltration, the most prominent of which was located beneath the anterior end of the left first rib and measured about 1.5 cm. in diameter. (Fig. 6). Cultures of the bone marrow were sterile.

On Saturday, July 28th, the authors visited this farm where specimens were obtained from the floor of the chicken house and Petri dishes were exposed to the air near the floor. All cultures for pathogenic fungi in the Clinical Laboratories at the University of Virginia were negative. A residuum of the specimen was sent to the Communicable Disease Center of the United States Public Health Service in Kansas City, Kansas.*

Since the second visit to the Pediatric Clinic on August 2, 1956, none of the members of this family has been seen at the University of Virginia Hospital. The public health physician collected a second specimen of blood for complement fixation tests about December 10th at which time the patients had moved into a neighboring district. Later the family migrated into an adjoining part of West Virginia and are said to be alive and well.

Discussion

At least 30 epidemics of a respiratory illness, which altogether involved more than 370 persons[4], are known to have followed the inhalation of dust in silos, chicken houses, belfries, caves, cellars, and even in the open air. Some of the "epidemics" have been proved to be due to *Histoplasma capsulatum*, while in others the final cultural link in the evidence has not been possible to obtain. The cases reported in this communication are examples of a dust-borne infection manifested by moderately severe systemic symptoms and evidence of generalized pulmonary involvement. Organisms could not be cultured from the patients at the times when they were seen but were recovered from the point source. The diagnosis was made from the familiar pattern of exposure to contaminated dust, subsequent mild to moderate illness, positive skin test, positive and changing complement-fixation tests and characteristics roentgenographic changes.

SUMMARY

An "epidemic" of histoplasmosis results when several persons become ill from generalization of a pulmonary infection incurred by simultaneous inhalation of dust containing the organism *Histoplasma capsulatum*. A number of such epidemics have been reported, involving almost 400 persons. For the most part these have occurred in the endemic area of central United States. The authors report an epidemic in a family from northern Virginia consisting of young parents and four children, five to 11 years of age, who were exposed at the same time to the dust raised during the cleaning of a

*Culture reported positive for Histoplasma capsulatum.

chicken house. In 10 to 12 days they became variably ill with fever, malaise, non-productive cough, irritability, weakness, nausea, anorexia, and headache. Roentgenograms of the chest showed pathology in all proportional to the degree of exposure and comparable to the severity of the symptoms. The only significant physical abnormalities were mild generalized adenopathy in the children and palpable liver in the father. The skin tests and complement fixation tests were positive in all six members of the family. Cultures of blood and marrow in the mother and children were negative for *H. capsulatum*, but this organism was ultimately recovered on culture from a specimen of the guano from the floor of the chicken house. The illness lasted about six weeks. The roentgenograms showed a tendency to improvement, but the family, who are migrants, have not been heard from for some months.

RESUMEN

Una epidemia de histoplasmosis resultó cuando varias personas enfermaron de una afección pulmonar generalizada después de la simultánea inhalación de polvos que contenían el organismo *Histoplasma capsulatum*. Se han relatado cierto número de epidemias que han incluido casi 400 personas. La mayoría han ocurrido en el área central de los Estados Unidos. Los autores relatan una epidemia en una familia del norte de Virginia, la que consistía en padre y madre jóvenes y cuatro hijos de 5 a 11 años de edad que se expusieron al mismo tiempo a polvo levantado al asear un gallinero. En un término de 10 a 12 días cayeron enfermos en forma variable, con fiebre, malestar, tos no productiva, irritabilidad, debilidad, náusea, anorexia y cefalalgia. Las radiografías del tórax mostraron cambios patológicos en todos, en proporción al grado de exposición y comparable a la gravedad de los síntomas. Las únicas anormalidades físicas fueron moderada adenopatía generalizada en los niños e hígado palpable en el padre. Las reacciones cutáneas y las de fijación del complemento fueron todas positivas en los seis miembros de la familia. Los cultivos de la sangre y de la médula ósea de la madre y de los niños, fueron negativas para el H. capsulatum pero este organismo fué encontrado en cultivo de una muestra de guano del piso del gallinero.

La enfermedad duró como seis semanas. La radiografía mostró tendencia a la meporía pero la familia que es de inmigrantes se ha perdido de vista por varios meses.

RESUME

Une "épidémie" d'histoplasmose survient lorsque plusieurs personnes deviennent malades après généralisation d'une contamination pulmonaire survenue à la suite d'une inhalation simultanée de poussières contenant *l'histoplasma capsulatum*. Un certain nombre d'épidémies ont été rapportées, atteignant non loin de 400 personnes. Elles sont survenues pour la plupart dans la zone endémique du centre des Etats-Unis. Les auteurs rapportent une épidémie dans une famille originaire du nord de la Virginie, ayant atteint de jeunes parents et quatre enfants, âgés de 5 à 11 ans, qui furent exposés en même temps à la poussière soulevée pendant la désinfection d'un poulailler. En dix à douze jours, ils furent atteints à des degrés divers de fièvres, malaise, toux non productive, irritabilité, faiblesse, nausées, anorexie et maux de tête. Des radiographies de la poitrine mon-

trèrent une atteinte proportionnelle au degré d'exposition et en rapport avec la sévérité des symptômes. Les seules anomalies significatives à l'examen physique furent une légère atteinte ganglionnaire généralisée chez les enfants, et un foie palpable chez le père. Les tests cutanés, et les tests de complément de fixation furent positifs chez les six membres de la famille. Les cultures sur le sang et la moelle chez la mère et les enfants furent négatives pour l'histoplasma capsulatum, mais ce germe fut finalement retrouvé en culture dans un échantillon du fumier recueilli sur le sol du poulailler. La maladie dura environ six semaines. Les radiographies montrèrent une tendance à l'amélioration, mais le famille n'a pas donné de ses nouvelles depuis quelques mois.

ZUSAMMENFASSUNG

Eine "Epidemie" von Histoplasmose kommt zustande, wenn mehrere Personen erkranken infölge einer Generalisation einer pulmonalen Infektion, die sie sich zugezogen haben durch gleichzeitige Inhalation von die Erreger (*Histoplasma capsulatum*) enthaltenden Staub.

Es liegen Berichte vor über eine Anzahl solcher Epidemien, die nahezu 400 Personen betreffen. Meistens traten sie in dem endemischen zentralen Bereich der USA auf. Die Verfasser berichten über eine Epidemie in einer Familie aus dem nördlichen Virginia. Sie bestand aus den noch jungen Eltern und 4 Kindern bis 5 und 11 Jahren, die zur gleichen Zeit Staub ausgegsetzt waren, der sich bei der Reinigung eines Huhnerhauses verbreitet hatte. Im Verlauf von 10-12 Tagen erkrankten sie in verschiedener Form mit Fieber, Unwohlsein, trockenem Husten, Reizbarkeit, Schwäche, Erbrechen, Appetitlosigkeit und Kopfweh. Thorax-Röntgenaufnahmen zeigten pathologische Veränderungen in allen Fällen, und zwar entsprechend dem Ausmass der Exposition und vergleichbar der Schwere der Symptome. Die einzige Veränderung von Bedeutung bei der physikalischen Untersuchung waren eine leichte allgemeine Lymphknotenempfindlichkeit bei den Kindern und eine tastbare Leber bei dem Vater. Die Hautproben und die Komplement-Bindungs-Reaktion waren bei allen 6 Familienmitgleidern positiv. Kulturen aus dem Blut und Mark bei der Mutter und den Kindern auf *Histoplasma Capsulatum* blieben negativ, aber der Erreger wurde schliesslich gefunden durch Kultur eines Guano-Präperates aus dem Gang des Hühnerhauses. Die Krankheitsdauer betrug 6 Wochen. Die Röntgenaufnahmen zeigten eine Tendenz zur Besserung, aber von der Familie—es handelte sich um Vagabunden—hat man seit einigen Monaten nichts mehr gehört.

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SECTION ON CARDIOVASCULAR DISEASES

Comparative Effects of Various Rauwolfia Alkaloids in Hypertension

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In 1942, Bhatia[1] pointed out the beneficial value of Rauwolfia serpentina in patients with high blood pressure. Since that time this agent, its alkaloids or related alkaloids, have all been employed successfully for the treatment of hypertension.

It is the purpose of this report to compare the effects of various Rauwolfia alkaloids in the treatment of this disease. The agents employed were 1) the alseroxylon fraction, 2) reserpine, 3) deserpidine, and 4) rescinnamine. Studies were made to determine the blood pressure response, the maximum dose which was well tolerated and the incidence of side effects.

Methods and Materials

Eighty patients with benign essential hypertension were studied. Their ages averaged 52 years (20 to 70) and 58 per cent were men. All were ambulatory out-patients of the hypertensive clinic who had been examined by the same observer at two to four week intervals for from two to five years.

All patients had received previous medication of various types for the treatment of their disease. They were accustomed to reporting the appearance or disappearance of symptoms. Blood pressure readings were taken after they had rested 20 minutes in the supine position. The lowest of three readings was recorded. The pressure was checked frequently by more than one examiner and a standard mercury manometer was employed. The average control systolic blood pressure for the entire group was 180 (142 to 237 mm. Hg.) and the average diastolic pressure was 111 (91 to 164) mm. Hg.

The control blood pressure readings were recorded after a reducing diet and non-specific measures had been employed for some months, and after the blood pressure had become stable.

A one month interval was allowed between the stopping of one drug and the administration of another so that all effects of the first drug would have been dissipated by the time the new agent was given. Neither the patient nor the physician knew which drug was being tested. The order in which the drugs were employed were 1) placebo, 2) reserpine, 3) the alseroxylon fraction of Rauwolfia serpentina, 4) deserpidine and 5) rescinnamine.

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Reserpine is a single alkaloid of Rauwolfia serpentina. The structural formula as reported by Mueller et al[2] is shown in Figure 1.

The alseroxylon fraction of Rauwolfia serpentina contains at least nine alkaloids which are standardized biologically for their hypotensive, bradycardic and sedative properties. They are also standardized chemically according to their ultraviolet and infrared absorption characteristics.[3]

Deserpidine is an alkaloid derived from the root of Rauwolfia canescens. Chemically, it is closely related to reserpine, lacking only the methoxy group at position 5 in ring A. The isolation of this alkaloid was first reported in 1955 by Stoll and Hoffman[4] who named it canescine.

Rescinnamine was first isolated by Klohs et al[5] and has been identified as the 3, 4, 5-trimethoxycinnamic acid ester of methyl reserpate.

Animal experiments have shown that reserpine, alseroxylon, deserpidine and recinnamine all are capable of depressing central cardiovascular reflexes. The carotid sinus pressor reflex is inhibited and the hypoxia pressor response is reversed. The pressor response which ordinarily follows electric stimulation of the afferent vagus nerve is lessened and an antiserotonin effect has also been demonstrated.

It has been stated that these agents possess an antiadrenal corticoid action, in that the hypertension produced by cortisone, DOCA and salt is decreased. These agents apparently have no effect on renal plasma flow or kidney function. There is no peripheral adrenergic blockade because epinephrine produces a greater rise in blood pressure after these agents than before. Also, Isuprel produces a greater fall in pressure and more tachycardia after Rauwolfia is given.

These drugs have no direct vasodilating action as intraarterial injection into the sympathectomized limb or the isolated paw of an animal does not increase the flow. There is no sympathetic ganglionic blockade and the carotid sinus is not sensitized.

Procedure

The patients were divided into four groups. Group 1, 20 patients who received a placebo; group 2, 20 who received reserpine followed by the alseroxylon fraction; group 3, 20 who received reserpine followed by rescinnamine, and group 4, 20 who received reserpine followed by deserpidine.

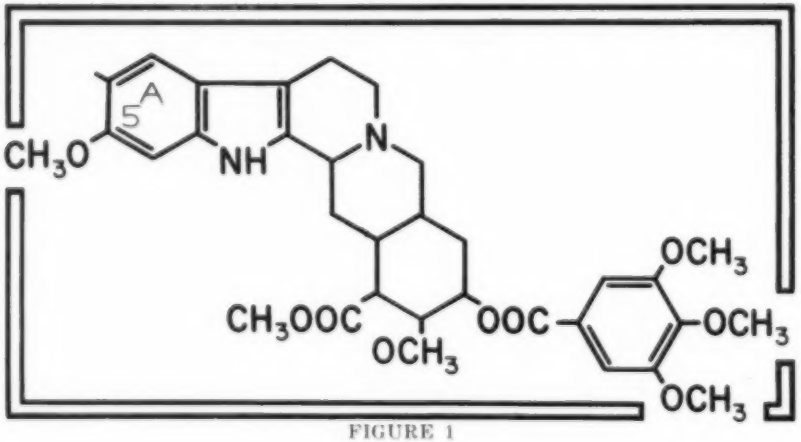

FIGURE 1

Results

Group 1: Effect of Placebo on Blood Pressure

Placebo tablets, one three times a day, were given for one month and blood pressure was measured before and after this therapy. The average fall in pressure was 11 mm. Hg. systolic, and 4 mm. Hg. diastolic. The smallest fall was none at all in both systolic and diastolic pressure; the greatest pressure drop was 34 mm. Hg. systolic, and 12 mm. Hg. diastolic.

Group 2: Comparison of Reserpine with Alseroxylon Fraction

The results of this study are shown in Table I. The maximum well tolerated dose of reserpine was established by giving the maximum amount of drug which the patients were willing to take over a long period of time. When obvious side effects were present, such as stuffiness of the nose, the dose was reduced to a comfortable level. This dosage was then employed for the test. It averaged 0.50 mg. daily (range 0.1 to 1.0). The study was continued for a period of one month after dosage had been established.

The average fall in blood pressure with reserpine was 23 mm. Hg. systolic, and 15 mm. Hg. diastolic. The smallest fall was 0 mm. Hg. systolic and 2 mm. Hg. diastolic, and the greatest fall 60 mm. Hg. systolic and 30 mm. Hg. diastolic. The side effects which occurred with the doses employed are shown in Table IV.

After one month, reserpine was stopped and no drug was given for a four-week period. The alseroxylon fraction of Rauwolfia serpentina was then administered in an average dose of 4.5 mg. per day (range 2 to 8 mg.). The average fall in pressure was similar to that with reserpine, being 26 mm. Hg. systolic, and 12 mm. Hg. diastolic. The side effects produced with this dosage of the medication are shown in Table IV. The hypotensive effects of these two agents were essentially the same.

Group 3: Comparison of Reserpine with Rescinnamine

The results are shown in Table II. The average dose of reserpine was 0.5 mm. a day (range 0.2 to 0.75 mg.). The average blood pressure fall was 20 mm. Hg. systolic and 15 mm. Hg. diastolic.

This may be compared with rescinnamine given in an average dose of 1.5 mg. (i.e., three times the dosage of reserpine). With rescinnamine the average fall was 8 mm. Hg. systolic, and 6 mm. Hg. diastolic. The side

TABLE I
COMPARISON OF RESERPINE WITH ALSEROXYLON FRACTION

	DRUG			
	Reserpine		Alseroxylon Fraction	
	Dose Mg./day	B.P. Change mm. Hg.	Dose Mg./day	B.P. Change mm. Hg.
Mean	0.50	—23/—15	4.5	—26/—12
Min.	0.10	0/— 2	2.0	— 5/0
Max.	1.00	—60/—30	8.0	—48/—22

TABLE II
COMPARISON OF RESERPINE WITH RESCINNAMINE

	DRUG			
	Reserpine		Rescinnamine	
	Dose Mg./day	B.P. Change mm. Hg.	Dose Mg./day	B.P. Change mm. Hg.
Mean	0.5	—20/—15	1.5	— 8/—6
Min.	0.2	0/0	1.0	0/0
Max.	0.75	—52/—28	2.5	—12/—9

effects with rescinnamine were low as compared with reserpine and the alseroxylon fraction and are shown in Table IV.

Group 4: Comparison of Reserpine with Reserpidine

Results from this group are shown in Table III. An average dosage of 0.25 mg. was employed for both reserpine and deserpidine (range 0.1 to 0.5 mg.). The average fall in blood pressure with reserpine was 19 mm. Hg. systolic, and 11 mm. Hg. diastolic. Results from deserpidine were closely comparable, the average reduction in blood pressure being 18 mm. Hg. systolic, and 9 mm. Hg. diastolic. The side effects are shown in Table IV.

Side Effects

Reserpine and the alseroxylon fraction had side effects which were similar in type and magnitude. The predominant symptom was lethargy, but nasal obstruction, dreams and muscle aching were also common.

Mental depression occurred in a significant percentage of patients and when present, necessitated stopping the drug or drastically reducing the dosage. Lethargy was more pronounced during the day when the medication was given in the morning. It was less pronounced when medication was given before bedtime.

Nasal obstruction was more disturbing when the medication was given before bedtime, because the post nasal discharge accumulated more readily when the patient was in the supine position. Dreams were more common when medication was given at night; however, even with a morning dose, they occurred in some patients. Muscle aching was often mild, and could

TABLE III
COMPARISON OF RESERPINE WITH DESERPIDINE

	DRUG			
	Reserpine		Deserpidine	
	Dose Mg./day	B.P. Change mm. Hg.	Dose Mg./day	B.P. Change mm. Hg.
Mean	0.25	—19/—11	0.25	—18/— 9
Min.	0.1	— 2/0	0.1	— 1/— 1
Max.	0.5	—38/—12	0.5	—32/—10

be improved by reducing the dosage slightly. Diarrhea was not common but when it occurred it was disturbing, and often necessitated stopping the drug.

Deserpidine showed a lower incidence of side effects (as far as lethargy and depression were concerned) as compared with reserpine and alseroxylon when deserpidine was given in the morning or during the day; however when it was given at night, restlessness, nervousness and insomnia were produced. The average fall in blood pressure with deserpidine was similar to that with reserpine. Similar findings have been reported by other workers, including Achor and Hanson.[6]

Rescinnamine given in the morning or evening had an exceedingly low incidence of all side effects, even though a large average dose of medication was employed (1.5 mg.).

Discussion

Studies of the effects of reserpine, alseroxylon, deserpidine and rescinnamine show that reserpine in an average dose of 0.5 mg. has the same hypotensive effect as 4.5 mg. of alseroxylon. The side effects of these two agents are similar. Rescinnamine in doses of 1.5 mg. has only minimal hypotensive effect as compared with 0.5 mg. of reserpine. Rescinnamine has almost no side effects when this dose of medication is employed. Nevertheless, rescinnamine does not appear to be a suitable agent for the treatment of hypertension, even though the incidence of side effects is low.

It is of interest that the *maximum* fall of systolic and diastolic blood pressure with rescinnamine was 12 mm. Hg. systolic, and 9 mm. Hg. diastolic. This occurred in a patient who received a dosage of 2.5 mg. This fall is even less than the *average* fall in pressure with reserpine (20 mm. Hg. systolic, and 15 mm. Hg. diastolic, with an average dose of 0.5 mg. daily). Also, the hypotensive effect of rescinnamine was quite irregular as only 40 per cent of the patients had a fall in pressure with rescinnamine, as compared to 88 per cent with reserpine.

The slight structural difference between reserpine and deserpidine is of interest. The lack of the methoxy group, in ring A in the latter, may account for the lower incidence of depression which was noted with this agent. Deserpidine, when given in the morning, showed a definitely lower incidence of lethargy, and depression was not encountered in any patient.

TABLE IV
INCIDENCE OF SIDE EFFECTS

	DRUGS			
Side Effects	Reserpine	Alseroxylon	Deserpidine	Rescinnamine
Lethargy	11	10	1	1
Nasal Obstruction	10	8	8	2
Dreams	8	7	3	1
Aching	8	7	3	0
Depression	3	3	0	1
Diarrhea	2	3	1	0

Nasal obstruction occurred with about the same frequency as with reserpine and alseroxylon. Dreams were definitely less common when deserpidine was given in the morning; however, a higher incidence of dreams than that shown in Table IV was encountered when the drug was given before bedtime.

SUMMARY

A study of the comparative hypotensive effects and side effects of reserpine, alseroxylon, deserpidine and rescinnamine revealed that:

1. Reserpine at an average dosage of 0.5 mg. and the alseroxylon fraction at an average dosage of 4.5 mg. both produced a satisfactory hypotensive response and the incidence of side effects of these agents when given during the day was similar quantitatively and qualitatively.

2. Deserpidine produced a hypotensive response which was similar to that of reserpine at the dosage employed and the incidence of side effects was less than that of reserpine (when the drug was given during the day) in that lethargy and depression were less common. When deserpidine was given at night nervousness and insomnia were produced.

3. Rescinnamine in an average dose of 1.5 mg. had the least hypotensive effect of any of the drugs tested.

Acknowledgment: The reserpine used in these studies is marketed under the trade name of Serpasil® and was supplied by the Ciba Company; the deserpidine is marketed under the trade name of Harmonyl® and was supplied by the Abbott Laboratory; the alseroxylon fraction is marketed under the trade name of Rauwiloid® and was supplied by the Riker Company. The rescinnamine also was supplied by the Riker Company. These studies were aided by grants from Mr. Henry Guidera and the aid from Mrs. Eva Kenoffel.

RESUMEN

Este es un estudio comparativo de los efectos hipotensores y colaterales de la reserpina:

1. A la dosis media de 0.5 mg. la reserpina y la fracción alseroxilón a la dosis media de 4.5 mg., ambos produjeron satisfactorios resultados hipotensores y la incidencia de efectos colaterales de estos agentes dados durante el día, fueron similares cualitativa y cuantitativamente.

2. La deserpidina produjo una respuesta hipotensora similar a la de la reserpina a las dosis empleadas y la incidencia de los efectos colaterales fué menor que con la reserpina (cuando la droga fué dada durante el día) en lo referente a que el letargo y la depresión fueron menos comunes.

3. La rescinamina a la dosis media de 1.5 mg. tuvo el menor efecto hipotensor que cualquiera de las drogas probadas.

RESUME

Une étude des effets hypotensifs comparatifs, et des effets toxiques de la réserpine, de l'alseroxylone, de la déserpidine et de la recinnamine révéla que:

1. la réserpine à une dose moyenne de 0,5 mg. et l'alséroxylone à la dose moyenne de 4,5 mg. ont tous les deux un effet hypotensif satisfaisant. La fréquence des effets toxiques de ces médications, quand elles étaient données au cours de la journée, était semblable quantitativement et qualitativement.

2. La déserpidine a un effet hypotensif semblable à celui de la réserpine aux doses utilisées, et la fréquence des effets toxiques a été moindre que celle de la réserpine (quand le produit était donné au cours de la journée):

la somnolence et la dépression étaient moins fréquentes. Quand la déserpidine a été administrée pendant la nuit, on a noté de la nervosité et de l'insomnie.

3. La rescinnamine à une dose moyenne de 1,5 mg. eut, de tous les produits essayés, l'action hypotensive la moins évidente.

ZUSAMMENFASSUNG

Eine Untersuchung der vergleichenden hypotonischen Wirkungen und Nebenwirkungen von Reserpin, Alseroxylon, Deserpidin und Recinnamin ergab, dass:

1. Reserpin bei einer durchschnittlichen Dosierung von 0,5 mg ebenso wie Alseroxylonfraktion in einer durchschnittlichen Dosierung von 4,5 mg zu einer befriedigend hypotonischen Antwort führen; die Nebenwirkungen dieser Stoffe bei Verabfolgung am Tage waren quantitativ und qualitativ ähnlich.

2. Deserpidin führte zu einer hypotonischen Antwort ähnlich derjenigen von Reserpin bei den verwandten Mengen, und das Vorkommen von Nebenwirkungen war geringer als beim Reserpin (wenn das Mittel am Tage gegeben wurde), insofern Lethargie und Depression weniger häufig auftraten. Wurde Deserpidin nachts gegeben, kam es zu Nervosität und Schlaflosigkeit.

3. Rescinamin mit einer durchschnittlichen Dosierung von 1,5 mg hatte den geringsten hypotonischen Effekt von allen geprüften Mitteln.

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Arteriovenous Fistula of the Lung*

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The problem of arteriovenous fistula of the lung is one of great interest to the internist, the thoracic surgeon and the physiologist. This interest exceeds the importance of this condition from a practical standpoint because it is distinctly a rare condition. Not many series are reported in the literature and those that are reported are not large. With the increased use of angiocardiography, however, this disease is being recognized more readily and there are now over 150 reported cases in the literature, most of them recognized in the past 15 years.

Over the past three years we have had four cases of arteriovenous fistula of the lung. It is the purpose in this paper to review the clinical aspects of the condition and present our experience in dealing with the anomaly.

Arteriovenous fistula or aneurysm of the lung is a congenital shunt between arteries and veins in the lung. This condition was recognized at autopsy as early as 1897,[1] but it was not until 1939 that a clinical, premortem diagnosis of arteriovenous fistula of the lung was made by Smith and Horton.[7] The true incidence of the anomaly is difficult to evaluate since small fistulas or aneurysms in the lung may easily escape diagnosis both clinically and by autopsy studies.[6] In the majority of cases the shunt is from a pulmonary artery to a pulmonary vein. One or more branches from the artery enter an aneurysmal sac which is drained by a greatly enlarged and tortuous vein. The size of the lesion may vary from small telangiectases to larger saccular, multilobulated aneurysms occupying the greater part of a lobe. In a series of 117 cases reviewed by Muri,[6] nearly half of the patients had two or more aneurysms large enough to be diagnosed clinically.

Some cases have been reported in which the arterial source of blood came from the descending part of the thoracic aorta or a branch or branches from the bronchial arteries.[5] In these cases cyanosis was not demonstrated since no right-to-left shunt with its excessive amounts of reduced hemoglobin was present. The arteriovenous shunt may be found anywhere in the lung but the majority have been found in the middle or lower lobes. One of our patients had a large lesion in the lingula of the left lung which was corrected by lingulectomy. Involvement of the thoracic wall by the arteriovenous anomaly, which greatly complicated the surgical correction,[2] has been described.

Diagnosis

The diagnosis of this condition is not difficult in a fully developed case. Cyanosis and clubbing of the fingers and toes, together with the presence on the roentgenogram of a round or lobulated density in the lung, are the essential aspects.

The cyanosis may reach extreme degrees depending upon the amount

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of arterial oxygen unsaturation and the hemoglobin value. When the fistula or aneurysm is composed of a pulmonary artery and pulmonary vein, a right-to-left shunt will be established leading to arterial oxygen unsaturation in the systemic circulation.[6] Arterial saturation as low as 59 per cent has been reported. This in turn causes a secondary, compensatory polycythemia with its rise of cell volume and hemoglobin value. In a series of 117 cases collected and reviewed by Muri, cyanosis and clubbing were present in approximately 75 per cent. Two of our patients, however, had a moderate anemia and no cyanosis or clubbing. In one case the anemia was secondary to an episode of profuse vaginal bleeding and in the other to moderate gastrointestinal bleeding. No specific cause for the bleeding could be demonstrated but it was assumed that telangiectasis or hemangiomas elsewhere in the viscera were responsible.

Telangiectasis on the skin or the visible mucous membranes is found in more than half of the cases and must be considered an important clue in the diagnosis. Many patients have reported recurrent epistaxis. Goldman[2] thought that arteriovenous fistula or aneurysm of the lung was a manifestation of hereditary hemorrhagic telangiectasis (Rendu-Osler-Weber disease). In the cases with marked cyanosis, variable neurologic symptoms may be present. These symptoms include headaches, syncope, thick speech, transient paresthesias, weakness of one side of the body, and even convulsions in some cases. The cause apparently is the associated anoxemia of the central nervous system. Small air emboli to the central nervous system have also been postulated as causative factors in the sudden appearance of neurologic signs.

Dyspnea is also a common complaint in the cyanotic patient but it is primarily dyspnea on exertion and less pronounced than would be expected

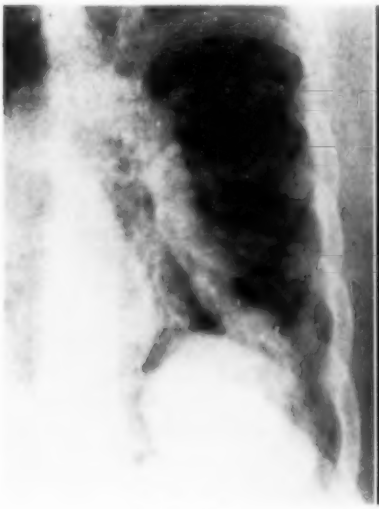

FIGURE 1

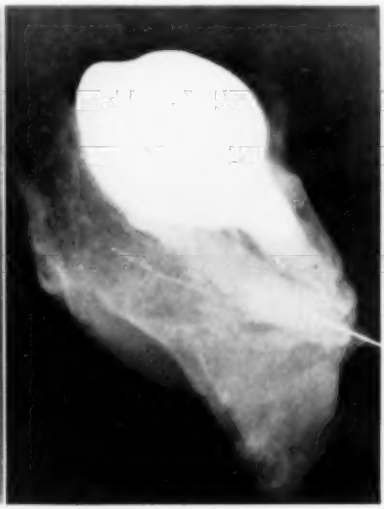

FIGURE 2

Figure 1: Angiocardiogram showing abnormally large pulmonary artery passing into aneurysmal sac at left base. (Published with the permission of the U. S. Naval Hospital, Chelsea, Massachusetts.)—*Figure 2:* Operative specimen of case shown in Figure 1. (Published with the permission of the U. S. Naval Hospital, Chelsea, Mass.)

with the degree of cyanosis present. The heart is usually normal in size unless some other unrelated cardiac disease is present. In patients with pulmonary arteriovenous fistula, right heart failure rarely develops. The overall vascular resistance in the lungs is not appreciably reduced and the cardiac output is usually within normal limits. If, however, the shunt is so large that 75 to 90 per cent of the blood passes through it, the pulmonary vascular resistance may be reduced significantly, the cardiac output raised and right ventricular hypertrophy and failure may develop.

In some cases, cyanosis and clubbing are not present because of the relatively small size of the shunt or because of bleeding elsewhere in the body. It has been estimated that cyanosis will not be visible until about 20 per cent of the blood passes through the shunt.[6] This figure corresponds to approximately 5 gm. of reduced hemoglobin per 100 cc. of blood. Therefore, although cyanosis may be present at birth, it is usually observed in the third or fourth decade when the fistula becomes large enough to shunt a sufficient amount of blood from the alveolar capillaries.

The heart sounds are normal unless some other unrelated valvular or congenital lesions are present. A murmur, however, is present in 50 per cent of the cases and may be associated with a palpable systolic thrill if the shunt is large enough and extends to the periphery of the involved lung. The murmur or bruit is heard over the site of the arteriovenous fistula and is usually systolic in time although in some cases it is continuous. In one of our cases in which the fistula was present in the lingula, the systolic murmur was located just outside the apex of the heart and

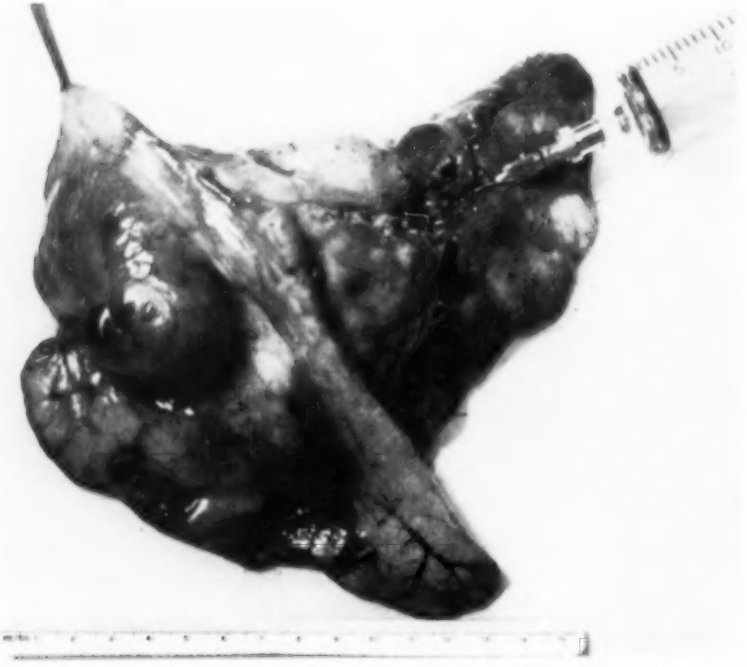

FIGURE 3: Specimen shown in Figure 2 injected with lipiodol. (Published with the permission of the U. S. Naval Hospital, Chelsea, Massachusetts.)

was originally mistaken for a mitral valvular murmur of insufficiency. Following lingulectomy, the systolic murmur disappeared.

Much can be learned from the roentgen studies which confirm the diagnosis. The most important finding indicating the possibility of an arteriovenous fistula in the lung is the presence of a shadow in the lung fields by roentgenograms. The density is round or lobulated and connected to the hilum by enlarged vascular shadows. The Valsalva and Müller's tests by changing the intrathoracic pressure have been helpful in demonstrating the vascular nature of the lesion in some cases.[4] By the Valsalva test, which is expiration against a closed glottis, the shadow will diminish. Conversely, by the Müller's test, which is inspiration against a closed glottis, the shadow will be increased.[4]

Angiocardiography, however, is the best method for demonstrating the vascular nature of the lesion (Fig. 1). The dye will concentrate in the aneurysm usually one or two seconds after it reaches the right atrium. It also may appear in the left atrium and aorta with unusual rapidity. It has been pointed out by others that other arteriovenous fistulas not suspected by the plain x-ray film may also be detected by this method.[6]

Other conditions causing extreme cyanosis and clubbing have to be excluded in the differential diagnosis. Congenital heart conditions with right-to-left shunts, particularly tetralogy of Fallot and Eisenmenger's syndrome with their overriding aorta have to be ruled out. With these, cardiac murmurs and catheterization studies will aid in establishing the correct diagnosis.

Polycythemia vera may be confused with arteriovenous fistula of the lung. In polycythemia vera, however, the older age group is usually involved, an enlarged spleen usually detected, and hematologic studies demonstrating a pancytosis aid in the correct diagnosis.

Severe cases of pulmonary fibrosis and emphysema may be confused with this condition, but careful x-ray and pulmonary function studies should be decisive in these cases. The important sign to keep in mind in arteriovenous fistula is the presence of a mass usually in the middle or lower lobes of the lung connected to the hilum by adjacent vessels, which can be demonstrated by angiocardiography.

Course

Muri has attempted a follow-up study of 50 patients who were not operated on. Some died of unrelated causes and others subsequently had surgery. In seven, however, the cause of death was rupture of the aneurysm into a bronchus or pleural cavity. Five patients died of brain abscess. This is a high percentage and compares with that in cases of congenital heart disease with right-to-left shunts. It has been postulated that paradoxical mycotic emboli by-passing the filters of the lung and lodging in the brain are responsible.

It is recommended that removal of the pulmonary arteriovenous fistula with its aneurysm be undertaken unless the surgical risk is prohibitive because of some other unrelated condition. Usually the removal can be accomplished by lobectomy. Because of the possibility that undetected multiple shunts exist which later may develop into larger aneurysms necessitating further resections, conservation of lung tissue is recommended.

SUMMARY

Arteriovenous fistula or aneurysm of the lung is a congenital shunt between arteries and veins in the lung. With the increased use of angiocardiography, the condition is being recognized more readily than before. In the majority of cases the shunt is from a pulmonary artery to a pulmonary vein.

The diagnosis is suggested by cyanosis and clubbing of the fingers and toes, together with the presence on the roentgenograms of a round or lobulated density in the lung. The cyanosis may reach extreme degrees depending upon the amount of arterial oxygen unsaturation and hemoglobin value. Telangiectasis on the skin or visible mucous membrane is found in more than half of the cases. In the cases with severe cyanosis, variable neurologic symptoms may be present. A murmur or bruit is present in 50 per cent of the cases and is heard over the site of the arteriovenous fistula.

Angiocardiography is the best method for demonstrating the vascular nature of the lesion in the lung. The dye will concentrate in the aneurysm one or two seconds after it reaches the right atrium.

It is recommended that removal of the pulmonary arteriovenous fistula with its aneurysm be undertaken unless the surgical risk is prohibitive because of some other unrelated condition. Usually the removal can be accomplished by lobectomy.

RESUMEN

La fístula arteriovenosa o aneurisma pulmonar es una intercomunicación congénita entre arterias y venas del pulmón. Con el uso creciente de la angiocardiografía este padecimiento se reconoce con más facilidad que antes. En la mayoría de los casos la intercomunicación es entre una arteria pulmonar y una vena pulmonar.

El diagnóstico es sugerido por la cianosis y los dedos hipocráticos en manos y pies así como la presencia en las radiografías de una densidad redonda o lobulada en el pulmón. La cianosis puede llegar a grados extremos según la cantidad de sangre arterial no saturada y la proporción de hemoglobina.

Se encuentran telangiectasia en la piel y en las mucosas visibles en más de la mitad de los casos. En aquéllos con cianosis acentuada puede haber síntomas neurológicos. Hay soplo o ruido en 50 por ciento de los enfermos y se ausculta sobre el lugar de fístula arteriovenosa.

El mejor método para demostrar la naturaleza vascular de la lesión es la angiocardiografía. El medio de contraste se concentra en el aneurisma uno o dos segundos después de que llega al atrio derecho.

Se recomienda la extirpación del aneurisma a menos que el riesgo operatorio lo contraindique a causa de alguna afección coexistente. Generalmente la extirpación se hace por lobectomía.

RESUME

La fistule artério-veineuse ou anévrysme artério-veineux du poumon est un shunt congénital entre les artères et les veines du poumon. Avec l'emploi accru de l'angiocardiographie, l'affection est plus facilement reconnue qu'auparavant. Dans la majorité des cas, le shunt va d'une artère pulmonaire à une veine pulmonaire.

Le diagnostic est évoqué par la cyanose et la déformation des doigts et des orteils, ainsi que par la présence sur les clichés d'une opacité arrondie ou lobulée dans le poumon. La cyanose peut atteindra des degrés extrêmes, dépendant du taux de la saturation oxygénée artérielle et de l'hémoglobine. Des télangiectasies au niveau de la peau ou des muqueuses visibles se trouvent dans plus de la moitié des cas. Dans les cas atteints de cyanose grave, des symptômes neurologiques variables peuvent exister. Un bruit ou souffle existe dans 50% des cas, et est perceptible au niveau de la fistule artérioveineuse.

L'angiocardiographie est la meilleure méthode pour mettre en évidence la nature vasculaire de la lésion pulmonaire. Le colorant se concentrera dans l'anévrysme une ou deux secondes après avoir atteint l'oreillette droite.

Il est conseillé d'enlever la fistule artérioveineuse pulmonaire avec son anévrysme à moins qu'il n'y ait un risque chirurgical en rapport avec quelque autre état. Habituellement l'exérèse comporte une lobectomie.

ZUSAMMENFASSUNG

Eine arterio-venöse Fistel oder Aneurysma der Lunge ist ein congenitaler Shunt zwischen Arterien und Venen in dr Lunge. Mit einer Zunahme der Verwendung der Angiocardiographie wird dieser Krankheitszustand häufiger als früher erkannt. In der Mehrzahl der Fälle liegt der Kurzschluss zwischen einer Pulmonalarterie und Pulmonalvene.

Die Diagnose lässt sich vermuten aus einer Zyanose, Trommelschlegelbildung von Fingern und Zehen zusammen mit dem Vorliegen einer Röntgenaufnahme einer runden oder gelappten Verdichtung in der Lunge. Die Zyanose kann extreme Grade erreichen, je nach dem Aussmass des arteriellen O_2-Defizits und des Haemoglobinwertes. In mehr als der Hälfte der Fälle findet man Telangiektasien der Haut oder sich baren Schleimhäut. In den Fällen mit schwerer Cyanose können variable neurologische Symptome vorliegen. Ein murmulndes Geräusch besteht in 50% der Fälle und ist über dem Sitz der arteriovenösen Fistel zu hören.

Die Angiocardiographie ist die beste Methode zum Nachweis der vasculären Natur des Lungenherdes. Das Kontrastmittel wird sich in dem Aneurysma ansammeln 1 oder 2 Sekunden, nachdem es den rechten Corhof erreicht hat.

Es wird empfohlen, dass die Entfernung der pulmonlaen arteriovenösen Fistel mit ihrem Aneurysma vorgenommen wird, sofern nicht das chirirgische Risiko dem entgegen steht aus anderen, nicht in Zusammenhang stehenden Gründen. Gewöhnlich lässt sich die Entfernung durch eine Lobektomie erreichen.

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The Quinidine Test Dose: Is It Warranted?

The significance of the Quinidine Test Dose (QTD) as a criterion for the use of quinidine in the treatment of auricular fibrillation is too often overestimated, misinterpreted, and misleading. All too frequently it leads to the indiscriminate use of the drug without apparent appreciation of its pharmacologic properties or the pathophysiology of the cardiac status being treated. As a result, an increasing number of case reports have appeared in the literature relating instances of convulsions, shock-like syndromes, and sudden deaths which have occurred during the course of treatment with or following the use of quinidine for the treatment of auricular fibrillation.[1-4]

What is the Quinidine Test Dose? The usual QTD is as follows: The patient for whom quinidine therapy is being contemplated is given an oral dose of 3 grains. Should this individual, following ingestion of the drug, show evidence of an idiosyncrasy manifested by marked nausea, vomiting, diarrhea, tinnitus, skin rash, etc., the drug is considered toxic and is discontinued. On the other hand, should the patient tolerate this initial dose, this is too often construed as a green light for an almost unrestrained continued use of quinidine.

What is the actual significance of the QTD? All it signifies is that the patient is either idiosyncratic to the effects of the drug or he can tolerate 3 grains of it. It does not indicate that the patient can tolerate any more than the initial dose without the possibility of suffering unfavorable effects.

However, this is the usual practice after the patient has shown a tolerance for the initial QTD. He is immediately given doses of quinidine at frequent short intervals, 2, 3, or more times the amount of the initial dose. This procedure is then continued until the cardiac irregularity being treated is restored to normal sinus rhythm or the patient shows signs of more or less marked toxicity. To say the least, this is a hazardous procedure. Because a patient may tolerate a small dose of quinidine without any untoward toxic manifestations is no sound pharmacologic reason for assuming that he can safely tolerate doses many times the size of the initial dose, given repeatedly at short intervals, without suffering toxic reactions. Some patients may well tolerate a small dose of the drug and yet manifest toxic symptoms when this same dose is repeated but once in too short a period of time. There are also those who can tolerate excessive amounts of quinidine without showing any ill effect whatsoever. Each individual has his own tolerance or threshold for the drug.

Not only has each individual a specific tolerance for a definite amount of the drug, depending upon the size of the dose and the rate of administration, but each individual will display his own characteristic signs and symptoms of toxicity when the threshold or tolerance for the drug has been exceeded. As the first evidence of exceeding the tolerance for the drug, some patients will complain of vertigo, nausea, vomiting, diarrhea,

tinnitus, skin rash, or any combination of these symptoms, while in others the first manifestation of toxicity will be displayed by convulsions, shock-like syndromes, or even sudden death. The individual reaction depends upon the relative sensitivity of the various organs and centers in the body to the toxic effects of quinidine, since they too have their own threshold or tolerance for the effects of the drug.

We have seen this not infrequently in the laboratory (Fig. 1).[5] In some dogs and cats, respiration ceased almost immediately after starting the intravenous injection and when only an insignificant amount of the drug had been administered. Soon thereafter, the blood pressure dropped precipitously, and the animal went into convulsions. The heart beat usually continued for approximately 2 minutes before it too would stop beating, unless the respiratory center recovered before the heart had ceased to function or artificial respiration was applied. Artificial respiration often proved successful in restoring the respiration.

This, I believe, is what happens in some patients. The respiratory center in these individuals, and less often the nodal centers of the heart, is particularly sensitive to the depressant effects of quinidine and is not prepared for the effect of sudden excessive doses. It can easily be understood why such patients, who may well tolerate a test dose of 3 grains of quinidine, will suddenly and without warning go into a convulsion or a shock-like syndrome, or perhaps even die suddenly, if, after receiving the initial small dose, they are given doses of 6, 9, or more grains at frequent short intervals.

The electrocardiogram and quinidine blood level determinations are frequently used as guides for dosage or signs of toxicity. In good hands, they may be helpful. However, some of the most dangerous toxic effects may occur before an electrocardiogram is taken or even when quinidine blood levels have been considered well within the normal range.

Paralysis of respiration is the most frequent underlying cause for the serious accidents and fatalities following indiscriminate use of quinidine. It would appear that not too much attention has been given to an important study reported some 30 years ago by Gordon, Matton, and Levine.[6] These investigators demonstrated the sensitivity of the respiratory center of the cat to the toxic effects of quinidine. They particularly noted that the toxic symptoms displayed by the animals following cessation of respiration, such as convulsions and shock, simulated the symptoms which they had seen in some of their patients in the hospital who were on quinidine therapy. They also showed that the rate of administration of the drug determined the degree of toxicity. We have confirmed the results of this experimental study many times.

How is one to guard against these serious toxic complications of quinidine therapy? Quinidine must be given in small doses. The initial dose is 3 grains (0.20 gm.) and the doses are administered at two hour intervals, gradually increasing the size and number based upon the patient's individual needs and reactions. In brief, the tentative schedule is as follows: one dose, of 3 grains, the first day, two doses the second, three doses the third, and four doses the fourth. The dose is increased on the fifth day to 5 grains (0.33 gm.) for three doses, and on the sixth day, four doses.

The seventh day consists of three doses of five grains and a fourth dose of 10 grains (0.65 gm.). The eighth day three 10 grain doses are administered. We never give more than 30 grains of quinidine in any one day. We have outlined this procedure many times since the publication of our first report in 1932 on the use of quinidine for the treatment of auricular fibrillation.[5, 7] Among the many hundreds of patients treated by us during the past 29 years, we have had but one known fatality which could definitely be attributed to quinidine toxicity.

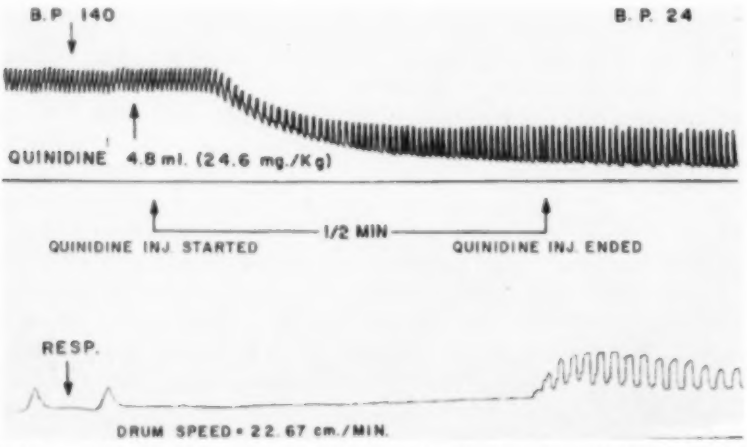

FIGURE 1: Note the immediate effect on respiration in a dog (12.7 kg.) following intravenous administration of 24.6 mg. of quinidine per kilogram of body weight. (Tambour manometer recording) Published in the Jour. of the Am. Med. Assoc. June 6, 1953, Vol. 152.

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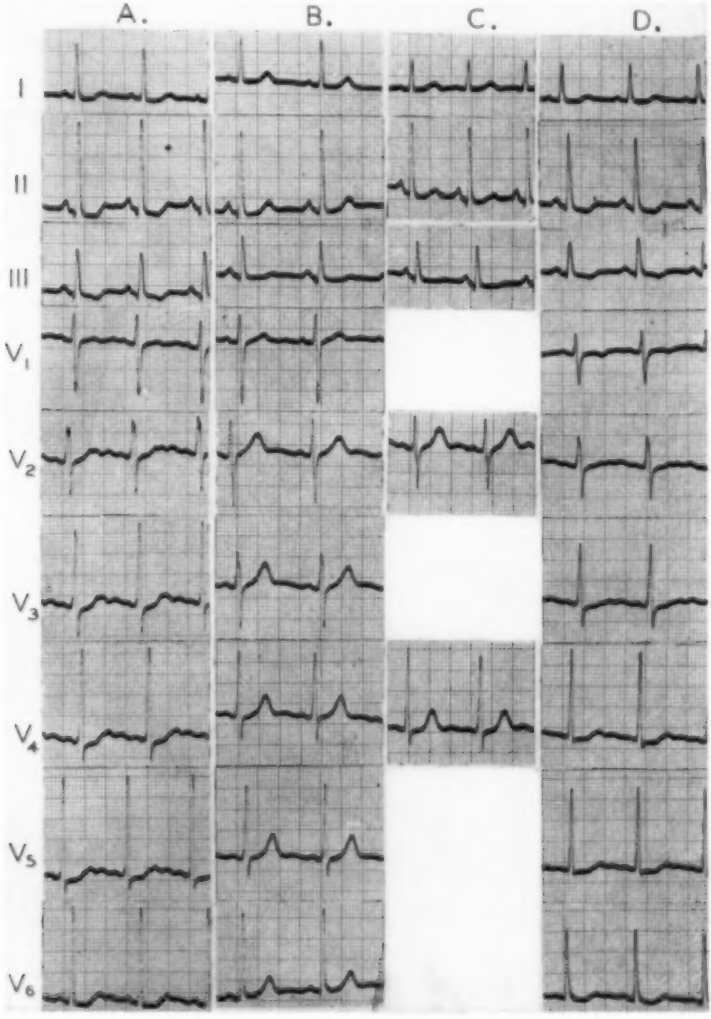
ELECTROCARDIOGRAM OF THE MONTH

The authors would be pleased to receive comment and controversy from the readers in relation to explanations offered.

During a routine "physical check-up" the electrocardiogram *A* was recorded from a 50 year old white woman. There was no symptom or sign of organic disease of any kind. Her blood pressure was 120/70. Note the RS-T segment shifts and the T waves in Leads II, III, V3, V4, V5 and V6. Another electrocardiogram, *B*, was made on the following day before breakfast in order to determine whether these changes resulted from the well-known effects of food. Immediately following the recording of the electrocardiogram *B* she was exercised vigorously and *C* was recorded. Then she was given breakfast. Electrocardiogram *D* was recorded 45 minutes after breakfast.



It is noted that the RS-T segment depression and the T wave changes are absent in the fasting electrocardiogram. They are hardly attributable to rapid rate, for the rate in *A* is but 90/minute. They do not appear after exercise (*C*) but they do appear after taking food. It is notable in this case, as in others, that the effects of exercise and the effect of food are different.

The question arises as to whether such changes induced by the taking of food may be regarded as non-pathologic changes. Since we have recorded such changes after the taking of food in 17 and 18 year old subjects who show no sign of disease of the heart and since this patient exhibited no symptom or sign of disease, cardiac or otherwise, the electrocardiographic changes are attributed to non-pathologic (food) effects.

A "routine" interpretation of the electrocardiogram *A* might have resulted in a diagnosis of heart disease. Had the patient had discomfort in the chest a diagnosis of coronary disease might have been made. The electrocardiogram *A* is also similar to many seen in the presence of left ventricular hypertrophy, and yet this diagnosis would also have been erroneous for the RS-T and T changes that suggest this diagnosis are absent when the patient is fasting.

All electrocardiograms that show such changes as those seen in *A* should be studied in the manner shown here. They may be but are *not necessarily due to heart disease*.

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X-RAY FILM OF THE MONTH

Clinical Information

The patient is a 15 year old asymptomatic white girl. She was admitted because of the findings on a routine chest film.

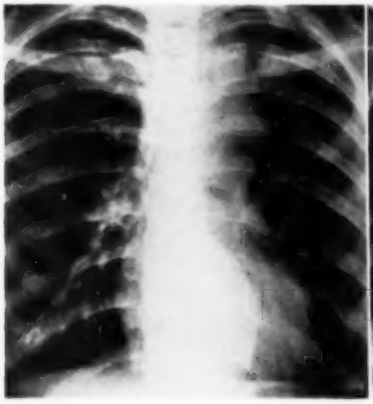

FIGURE 1

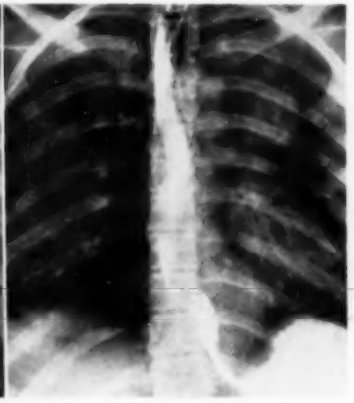

FIGURE 2

Figure 1: Admission chest film.—*Figure 2:* Bucky film.

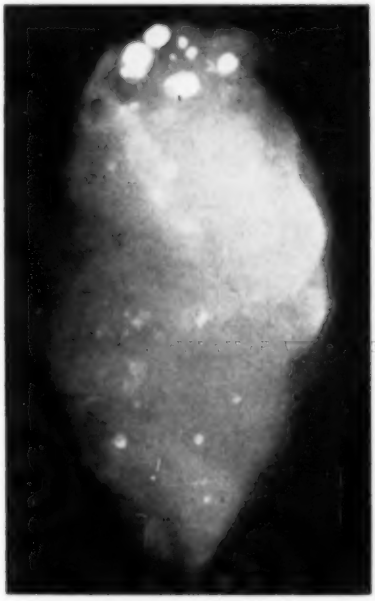

FIGURE 3: Roentgenogram of surgically resected lower mass.

Answer on page 434.

ANSWER

Multiple Hemangiomas of Mediastinum

The chest film reveals lobulated superior and posterior mediastinal masses which project to the left of the midline. Within the masses phleboliths are seen. On this basis a diagnosis of multiple hemangiomas of the mediastinum was made, and was confirmed at operation.

Only 19 proved cases of hemangioma of the mediastinum had been reported in the literature prior to 1955. They have been found at various ages. The patient may be entirely asymptomatic or may have any of a variety of complaints referable to the chest. Hemangiomas may be encapsulated, locally infiltrative, or frankly malignant. They may be multiple, as in the present case. They are more frequent in the anterior and superior mediastinum than in the posterior mediastinum. The demonstration of phleboliths within the mass is considered to be diagnostic of hemangioma.

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The Surgical Treatment of Mitral Stenosis*

Report of the Section on Cardiovascular Surgery of the American College of Chest Physicians

This report is based upon the response of 37 members of the advisory committee to this section regarding 10,000 operated patients.

It is now ten years since the first modern type operation for mitral stenosis was reported with a demonstration of the patient at the annual meeting of this College.[1] Since then, many thousands of patients have been operated for mitral stenosis, nearly always by the same technical method (although often under a different terminology). More recently, certain surgeons have adopted the right-sided approach and a new concept and method of mobilization of the stenotic valve (neostrophingic), while others have turned to open heart surgery using total cardiopulmonary bypass. However, these are relatively new innovations, the ultimate results of which are not yet evident.

In evaluating the merits of a specific type of treatment for any given disease entity, it is essential to know the outlook for the untreated patient. The operative risks and complications entailed in definitive measures then may be established upon the basis of early medical or surgical experience. However, the ultimate results of such treatment often cannot be assessed until after the passage of a long period of time—perhaps the span of a normal lifetime. Until then, one must be content periodically to observe the clinical trends and, from them, to interpolate the probable eventual fate of the subjects.

While mitral stenosis is a diagnostic entity of great antiquity (first described by De Vieussens[2] in 1705), controversy still exists as to the fate of the patient who is not treated surgically. Soloff and associates[3] are so skeptical of the possible benefits of surgical procedures as to ascribe them largely to psychosomatic suggestion and to more intensive ancillary medical administrations. On the other hand, Olesen,[4] from a study of 228 patients with mitral stenosis, has reported a 49 per cent mortality in Group III (New York Heart Association classification) cases within seven years and a 94 per cent mortality in Group IV cases within six years. And Bigelow and Greenwood[5] in a study of 171 patients have observed that after the appearance of (1) "severe pulmonary congestion," (2) right heart failure, or (3) atrial fibrillation, 16 per cent are dead within six months and 50 per cent die within five years. Twenty per cent may survive for as long as 15 years but then are severely disabled.

Operative Mortality

While the individual reports of operative mortality show great variation (from 1.5 per cent to 14 per cent), depending in large part upon the selection of cases for surgery, the over-all operative (hospital) mortality in this compilation was 6.8 per cent (Table I). This compares with a personal (left-sided closed technique) series consisting of 1,588 patients operated by the chairman of your Section (C.P.B.) in which the hospital

*Report of the Section on Cardiovascular Surgery. Presented at the 24th Annual Meeting, American College of Chest Physicians, San Francisco, June 18-22, 1958.

TABLE I—OPERATIVE (HOSPITAL) MORTALITY
37 Clinics Reporting

		Pure Mitral Stenosis	Preponderant Mitral Stenosis	Complicated Mitral Stenosis
	Per Cent	Per Cent	Per Cent	Per Cent
Total Cases	10,000 (100)	7,165 (72)	2,604 (26)	231 (2)
Mortality	679 (6.8)	418 (5.8)	221 (8.4)	40 (17.3)

mortality was 7.3 per cent. It is evident that in spite of bland assumptions to the contrary, there remains associated with this type of surgery a significant operative risk. Undoubtedly this might be reduced to any preselected level by restricting the case selection to those patients who are in relatively good condition. However, this very process of limitation necessarily must deprive many individuals in desperate need of surgical help of their only chance for rehabilitation. It would seem preferable either to devise a method by which we may reduce the severity of the operative and postoperative stress or, conversely, to improve the patient's ability to withstand it. In practice, after appropriate medical preparation, the latter may be accomplished by supporting the patient's circulation by artificial (mechanical) means with a total (open) or subtotal (closed) circulatory bypass system such as is being practiced now in some centers.

Results of Operation

Thirty-four of the cooperating clinics have evaluated their patients six months after surgery. The findings are summarized in Table II-A. The late results are somewhat harder to elicit. Ten clinics have reported upon the condition of a small number of patients (342) surviving five years after operation (Table II-B). Unfortunately, we are not sure how many patients failed to survive for this period of time, how many have been lost to follow-up, and how many have suffered from recurrence of the valvular obstruction, perhaps requiring re-operation. In the personal experience of your Section chairman (C.P.B.), the known mortality during the first five years after surgery has been 20.5 per cent. More than half (13 per cent) of this has been due to cardiac disease. Seven per cent of the patients have been lost to follow-up. There has been a 10 per cent

TABLE II-A—OPERATIVE RESULTS EARLY (6 mos.)
34 Clinics Reporting

Total Cases	Good	Improved	Poor
5,482	4,085 (75 per cent)	1,048 (19 per cent)	349 (6 per cent)

TABLE II-B—OPERATIVE RESULTS LATE (5 yrs.)
10 Clinics Reporting

Total Cases (Alive)	Good	Improved	Poor
342	240 (70.2 per cent)	87 (25.5 per cent)	15 (4.3 per cent)

incidence of recurrence of mitral obstruction within five years, and approximately half of these cases have been subjected to re-operation (for the most part, successfully).

Operative Technique and Accomplishments

Unfortunately, there has been a certain amount of variation in the operative techniques used in the cooperating clinics. In part, this has been related to a differing incidence of employment of a valvulotome (of several types), of a purely splitting (digital pressure) technique, and of a combination of these techniques. Many heated arguments have been generated at an earlier period over the question of the necessity for the use of a valvulotome. Today, nearly all surgeons attempt first to split the valve digitally and reserve the valvulotome for individuals in whom this effort fails. Even then, once the dense scar tissue about the valve margin has been divided, it often will be found possible to continue the mobilization digitally. More pertinent perhaps, with regard to technical variation, is a consideration of the direction and the extent of the valve separation.

Another important question concerns itself with the number of commissures which have been opened. A unicommissural separation of the valve provides neither the adequacy of aperture nor the freer mobility which attends an extensive bicommissural procedure. An attempt is made to indicate the extent to which these various factors might influence results in Tables III-A and III-B.

TABLE III-A—OPERATIVE TECHNIQUE EMPLOYED
37 Clinics Reporting

Technique	Total Cases	Pure Mitral Stenosis	Preponderant Mitral Stenosis	Complicated Mitral Stenosis
	Per Cent	Per Cent	Per Cent	Per Cent
	10,000	7,165	2,604	231
Finger Only	5,502 (55)	3,872 (54)	1,503 (57.7)	127 (54.9)
Valvulotome*	3,899 (39)	2,749 (38.4)	1,080 (41.8)	70 (30.3)
Other**	599 (6)	544 (7.6)	21 (0.5)	34 (14.8)

*Usually with some associated digital manipulations.
**Mechanical Dilator, Punch, etc.

TABLE III-B—VALVE MOBILIZATION ACCOMPLISHED
30 Clinics Reporting

	Total Cases	Pure Mitral Stenosis	Preponderant Mitral Stenosis	Complicated Mitral Stenosis
	Per Cent	Per Cent	Per Cent	Per Cent
	7,132	4,822	2,143	167
One Commissure Opened	2,738 (38.4)	1,891 (39.2)	736 (32.9)	111 (66.4)
Both Commissures Opened	4,250 (59.5)	2,832 (58.7)	1,370 (63.9)	48 (28.7)
Valve Dilated Only	144 (2.1)	99 (2.1)	37 (3.2)	8 (4.9)

"Subvalvular Stenosis"

Gradually it has become appreciated that thickening and cross-fusion of the chordopapillary supporting structures represents a common, perhaps a constant element in the pattern of rheumatic mitral valvulitis. However, it is of widely variable significance in individual cases of mitral stenosis, sometimes being physiologically negligible, while in other instances it may represent the major factor in the obstruction. Generally it merely reinforces the primary leaflet stenosis and, therefore, has been designated as "secondary" stenosis. Recognition at surgery depends upon the severity of the process and assiduity with which its presence is sought by the operating surgeon. The frequency of reported recognition in this study has varied from zero to 63 per cent. The over-all recognition and the effectiveness of treatment of the subvalvular stenosis (digital or instrumental efforts to separate the cross-fused structures into "mural" and "septal" components) is depicted in Table IV.

Operatively Produced Mitral Regurgitation

While in a theoretically ideal operation no new valvular incompetence should be produced and any pre-existing one should not be aggravated by a proper valvular mobilization, it is obvious that surgeons cannot always maintain this ideal.

One of the surgeon's best assurances that he is accomplishing a proper separation of the valve is the continued absence of a palpable jet of insufficiency. However, this very concept implies that logically he might continue his efforts at mobilization until the first beginning of such a jet becomes detectable. Its presence then would indicate either that the line of actual cleavage had begun to deviate from the ideal one or that the limits of permissible cleavage had been exceeded slightly. In either case, this would be interpreted as a signal to terminate all manipulations at this particular extremity of the valve.

Such minute degrees of valvular incompetence are insignificant clinically. At worst, they may produce an audible systolic murmur. In time, most of them tend to diminish and may become nonexistent either because of thickening of the cut valve edges or as a result of the Venturi effect by which the slightly divergent valve margins are drawn together by the "aspirating" effect of the transvalvular blood flow during systole.

However, more serious grades of incompetence also may be produced. Wide section of the continuity of the "septal leaflet," detachment of a "cusp" from the annulus fibrosus or division of an important portion of the chordopapillary supporting system may produce devastating, perhaps lethal regurgitation. Inadvertent perforation of the valve substance usually is somewhat less serious unless a very severe laceration is produced.

TABLE IV
RECOGNITION AND RELIEF OF SUBVALVULAR STENOSIS
25 Clinics Reporting

Total Cases	Subvalvular Stenosis Recognized	Relieved
6,157	569 (9.7 Per Cent)	456 (80.1 Per Cent of recognized)

Inadvertent section of the usually thick and rigid "mural leaflet" may be an insignificant injury since the hard fixed margins usually do not tend to separate and ordinarily are incapable of prolapse. Unlike that type of regurgitation which occurs along or at the extremity of the line of cleavage and which tends to become less postoperatively, significant incompetence of the various latter types tends to become aggravated with the passage of time. Chiefly, this is due to "overstretch" of the "annulus fibrosus" which is produced by dilatation of the left ventricle in its attempts to compensate for the valvular leak.

The incidence of creation or aggravation of mitral regurgitation in their cases has been indicated by all 37 contributing authors (Table V).

Prolonged or Recurrent Postoperative Febrile Reaction

Postoperatively, a significant number of patients who have survived surgery of the mitral valve suffer a febrile course which would seem to be of longer duration and associated with more serious distress than the magnitude of the procedure would seem to justify. In some cases this appears as a prolonged continuation of the "normal" postoperative febrile response. In others it appears, *de novo*, after the elapse of some weeks or months. Some patients present a cyclic course of exacerbations and remissions. In a certain proportion, this fever is associated with malaise, joint pains, increased sedimentation rate, leucocytosis, etc. Most observers state that it may be relieved dramatically by administration of any of the various "steroid" substances (A.C.T.H., cortisone, etc.). Since these drugs may influence favorably the temperature and course of rheumatic fever (although they were introduced originally as general "anti-stress" agents), and since mitral stenosis usually is a late result of rheumatic fever, Soloff and associates[3, 6] have assumed that such a reaction represents a recrudescence of rheumatic activity and have designated it as "postcommissurotomy syndrome." Others have objected to this conclusion on the basis that the various (admittedly nonspecific) humoral and serologic tests (antihyaluronidase, antistreptolysin titer, heomolysin level) which show elevated values in the "rheumatic state" rarely show a significant increase during the course of the "postcommissurotomy syndrome." Furthermore, similar febrile episodes may be noted following cardiac surgery for nonrheumatic conditions such as congenital heart lesions and coronary artery disease and are equally responsive to steroid administration. Not infrequently the temperature elevation may be relieved by

TABLE V
INCIDENCE OF OPERATIVELY CREATED REGURGITATION
37 Clinics Reporting

	Total Cases	Pure Mitral Stenosis	Preponderant Mitral Stenosis	Complicated Mitral Stenosis
		Per Cent	Per Cent	Per Cent
	10,000	7,165	2,604	231
Slight	1,343 (13.4)	923 (12.9)	390 (14.9)	30 (13)
Moderate to Severe	210 (2.1)	124 (1.7)	86 (3.3)	

TABLE VI-A
INCIDENCE OF PROLONGED POSTOPERATIVE FEBRILE REACTION

	Total Cases Per Cent	Pure Mitral Stenosis Per Cent	Preponderant Mitral Stenosis Per Cent	Complicated Mitral Stenosis Per Cent
	10,000	7,165	2,604	231
Febrile Response	812 (8.1)	418 (5.8)	221 (8.5)	40 (17.3)

needle aspiration, dark blood-stained fluid being removed from the pericardium or pleural cavity.

The exact frequency of occurrence of these episodes is difficult to ascertain because different clinics employ differing criteria for diagnosis. The reported incidence in this series is shown in Table VI-A. Each reporting author was asked to express an opinion as to the probable cause and the answers are compiled in Table VI-B.

Operatively Produced Systemic Arterial Embolization

Embolism which occurs at the time of surgical intervention for mitral stenosis is a distressing and not infrequently fatal complication of this type of surgery. Most authors feel that it may be produced either by dislodgement of a loosely attached particle of thrombotic material from the left atrial appendage or lateral atrial wall, or by fragmentation of a zone of calcific encrustation upon the stenotic valve. Hence the incidence of this complication depends upon the incidence of atrial thrombosis, the incidence of valvular calcification, the operative approach (whether through the possibly clotted appendage (left-sided approach) or from the septal aspect of the left atrium (right-sided approach), the specific operative technique employed (rapid and limited versus persistent and extensive), and upon certain "prophylactic" measures such as temporary constriction of the carotid arteries and evacuation of loosely attached clots from the atrium by "flush-out" or aspiration. Table VII reveals the overall incidence of systemic arterial embolization in 4,463 patients operated at nineteen clinics. In a personal series of one of us (C.P.B.), the incidence of operatively produced arterial embolization was 8.3 per cent in 659 patients with chronic atrial fibrillation and only 2.5 per cent among 754 patients with normal sinus rhythm.

Abolition of the Diastolic Murmur of Mitral Stenosis

While one hears many eminent cardiologists state that the characteristic diastolic murmur of mitral stenosis never is abolished by valvular surgery, it is interesting that fourteen of the authors who filled out the full

TABLE VI-B
OPINION OF REPORTING AUTHORS (37) AS TO CAUSE OF PROLONGED POSTOPERATIVE FEBRILE REACTION

Rheumatic	Not Rheumatic	Undecided
14	16	7

TABLE VII
EMBOLISM WITH RESPECT TO ATRIAL THROMBOSIS AND VALVULAR CALCIFICATION
19 Clinics Reporting

		Per Cent
Total Cases	4,463	
History of Preoperative Embolism	586	(13.1)
Atrial Fibrillation	1,343	(41.9)
Atrial Thrombosis Recognized at Operation		
Appendageal	727	(16.3)
True Atrial	211	(4.7)
Valve Calcification Recognized at Operation	1,073	(24)
Embolization Produced at Operation		
Cerebral		
Fatal	74	(1.6)
Nonfatal	84	(1.9)
Peripheral		
Fatal	54	(1.2)
Nonfatal	34	(0.6)
Late Embolization (3 weeks or longer postoperatively)	73	(1.6)

questionnaire reported an 8.1 per cent incidence of abolition of this murmur in a series of more than 3,000 cases (Table VIII).

Influence of Surgery Upon Heart Size

Much controversy has developed over the issue of alteration in heart size. Actually, since it is unusual for mitral stenosis to be relieved completely or even largely by the older commissurotomy type procedure, one should not expect a great reduction in heart size following such an operation. Increase in heart size might be attributed to progression in the course of the disease or to the inadvertent creation of significant regurgitation. Fourteen authors have analyzed 2,849 cases in this respect with the results shown in Table IX.

Recurrence of Mitral Obstruction

While it is generally realized that obstruction of the mitral orifice developing at some time following effective valvular surgery may be the result of a simple hardening of the margins of a previously flexible valve, in a large percentage of cases true refusion of the separated commissures has been demonstrated either at operation or at autopsy. Thirty one of our Advisory Board members reported a proved incidence of recurrent mitral

TABLE VIII
INCIDENCE OF ABOLITION OF THE DIASTOLIC MURMUR
14 Clinics Reporting

Total Cases	Diastolic Murmur Abolished
3,072	251 (8.1 Per Cent)

TABLE IX
ALTERATIONS IN HEART SIZE PRODUCED BY OPERATION
14 Clinics Reporting

Total Cases	No Change	Heart Size Reduced	Heart Size Increased
2,849	1,784 (62.6 Per Cent)	732 (25.7 Per Cent)	333 (11.7 Per Cent)

stenosis to date of 2.8 per cent developing among 8,638 operated patients. Undoubtedly this number will increase significantly with the passage of further time. Most of the reporting authors estimated the eventual incidence of restenosis following surgery at about 5 per cent. Five thought it would amount to 10 per cent. One felt that the ultimate rate would be about 50 per cent. Twenty-three of them felt the chief cause of recurrent mitral obstruction to be incomplete mobilization of the valve at the time of the first operation (Table X). Seven believe that rheumatic activity at the time of operation or subsequently is the chief cause of this complication, and 10 others consider this factor an occasional cause of restenosis. Five authors felt that the extreme state of valvular pathology (including calcification) sometimes encountered played a significant part in recurrence of the obstruction. Obviously it is not possible to differentiate clearly between these cases and those in which incomplete mobilization of the valve is responsible since the most pathological valves are the ones which are most difficult to mobilize.

Indications and Contra-Indications to Surgery for Mitral Stenosis

From the response to the questionnaires, it was evident that all of the reporting authors feel that the anatomical existence of significant mitral stenosis in itself constitutes sufficient indication for surgery in the absence of an appropriate contra-indication. As might have been expected, the most commonly mentioned contra-indications were rheumatic activity, severe myocardial disease, subacute bacterial infection, associated multivalvular disease, and mitral regurgitation (Table XI).

TABLE X
RECURRENT MITRAL OBSTRUCTION
31 Clinics Reporting*

Total Cases	8,638
Restenosis Proved (to date)	244
Estimation of a Rate of Recurrence	
Less Than 5 Per Cent	5
5 Per Cent	10
10 Per Cent	5
Over 10 Per Cent	3
Noncommittal	8
Assumption as to Cause of the Restenosis	
Incomplete Mobilization of the Valve	23
Rheumatic Activity	7-10
Extremes of Valve Pathology	5

*Some authors feel that restenosis may be caused by more than one factor; hence, total reports exceed 31.

TABLE XI
CONTRA-INDICATIONS TO SURGERY FOR MITRAL STENOSIS
16 Clinics Reporting

Acute or Subacute Rheumatic Activity	10
Severe Myocardial Disease (Intractable Heart Failure)	9
Associated Severe (Incorrectable) Disease of Other Valves	6
Subacute Bacterial Infection (Until Cured)	4
Serious Grade of Associated Mitral Regurgitation	5
Serious or Fatal Extracardiac Disease (Cancer, Emphysema, Debility, etc.)	4
Advanced Age (Usually over 65)	3
Recent Embolic Episode	3
Mildness of Symptoms (Grade I Cases)	3
Chronic Liver Disease (Congestive)	1

Satisfaction with the Current Operative Procedures for Mitral Stenosis

Each member of the Advisory Committee was asked if he was satisfied with the results of surgery for mitral stenosis. The comments are tabulated in Table XII. It is evident that one quarter of these authors are dissatisfied with the accomplishments of the standard operation for mitral stenosis (using the left-sided approach) and that another quarter give but a qualified approval. This is a finding of great significance when one considers the new approaches which are being suggested today (neostrophingic mobilization and open-heart techniques).

Summary and Conclusions

While the closed left-sided operation for mitral stenosis is well established and is currently being practiced in most of the leading clinics, it has not proved itself completely satisfactory even to the operating surgeons themselves. The operative mortality continues to stand at about 7 per cent. There is an attending incidence of created insufficiency of about 15 per cent, most of which is considered slight or clinically insignificant. There is a prolonged febrile postoperative course in about 8 per cent. Less than half of the reporting surgeons consider this to be of rheumatic origin. Systemic arterial embolization complicates 5 per cent of these operations, slightly more than half proving fatal. The diastolic murmur of mitral stenosis is abolished in 8 per cent. In most cases no change is noted in heart size. Most of the authors failed to report the exact incidence of rhythmic changes following surgery. However, many expressed the generalization that surgery did not seem permanently to alter the basic preoperative rhythm.

Recurrence of mitral obstruction can and does occur after the passage of several years. Most authors think its over-all incidence will be 5-10 per

TABLE XII
SATISFACTION WITH RESULTS OF SURGERY
37 Clinics Reporting

Satisfied	Dissatisfied	Qualified Approval
20	9	8

cent. The majority attribute its development to incomplete mobilization of the valve, although some feel that continued rheumatic activity may produce it.

One may justifiably conclude that mitral commissurotomy, as currently performed, has proved to be a moderately satisfactory procedure with a somewhat higher mortality and incidence of complications than was anticipated initially. The need for an operative method which can achieve a better mobilization of the valve with less risk is clearly evident.

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College Chapter News

FLORIDA CHAPTER

The annual meeting of the Florida Chapter will be held at the Americana Hotel, Bal Harbor, on Sunday, May 3. Following is the program:

8:40 a.m. Business meeting

9:00 a.m. "Inhalation Therapy in a Modern Hospital, A New Approach"
James Traitz, Coral Gables
Discussor: Allen Armstrong, Charlottesville, Virginia

"Vocal Cord Paralysis Related to Lesions in the Neck and Thorax"
Nathaniel M. Levin, Miami
Discussor: James Moody, Orlando

"Effect of Molar Lactate in Quinidine and Procaine Amide Intoxication"
Fred Wasserman, Miami
Discussor: James S. Jewett, Coral Gables

"Resection in Pulmonary Tuberculosis"
Clemente Oca, Lantona
Discussor: Hawley Seiler, Tampa

"Intestinal Duplication Cyst of the Abdominal Wall Present in the Thorax"
Harold C. Spear, Miami

"Effects of Respiratory Obstruction on the Ventilatory Response to Inhaled Carbon Dioxide"
Philip Samet, Miami Beach
Discussor: Asher Marks, Miami

Emphysema Panel
Moderator: George Baum, Coral Gables
Panel: Jerome Benson, Miami Beach; Asher Marks, Miami; Mark W. Wolcott, Coral Gables

12:00 noon Luncheon and business meeting

1:00 p.m. "Histoplasmosis"
Michael L. Furcolow, Kansas City, Kansas

"Auricular Tumors"
Martin Bell, Dallas, Texas
Discussor: Francisco Hernandez, Miami

X-ray Seminar (those in attendance are requested to bring x-ray films for discussion after a brief pertinent history)

GEORGIA CHAPTER

The annual meeting of the Georgia Chapter will be held on May 18 at the Bon Air Hotel, Augusta, in conjunction with the meeting of the Medical Association of Georgia, May 17-20. The chapter meeting will open with a joint luncheon with the Georgia Trudeau Society at 1 p.m. Following is the program:

2:30 p.m. "Choice of Diuretics"
Thomas Findley, Augusta

"Liver Function Tests—The Mechanism and Meaning"
John F. Galambos, Atlanta

"An Atherogenic Profile—Its Use in Managing the Coronary Patient"
Curtis G. Hames, Claxton, Georgia

"The Problem of Venous Thrombosis and Pulmonary Embolism"
Edgar A. Hines, Jr., Rochester, Minnesota

"Hypersensitivity Reactions to Penicillin"
Edward C. Evans, Atlanta

"Pyloric Channel Ulcer"
Thomas J. Anderson, Jr., Atlanta

ILLINOIS CHAPTER

The Illinois Chapter will hold its annual meeting at the Sherman Hotel, Chicago, on May 20. The following program will be presented:

9:00 a.m. "What's the Diagnosis?"
(Case presentations by various Chicago institutions)

"Tuberculosis Enterocolitis and Other Obstructive Lesions of the Bowel"
Leroy H. Berard, Chicago

"Cycloserine in High Dosage in Salvage Cases of Pulmonary Tuberculosis"
Marjorie M. Pyle, Karl H. Pfuetze, William R. Barclay, and John E. Kisak, Chicago
"On the Pulmonary Hypertension Associated with Defects of the Interatrial and Interventricular Septa"
H. J. C. Swan, Rochester, Minnesota

KANSAS CHAPTER

The Kansas Chapter will hold its annual meeting in Topeka, May 4 at the Jayhawk Hotel. Following is the program:

4:00 p.m. Robert M. Brooker, Topeka, Chapter President, presiding
"Resistant Asthma"
Ralph Hale, Wichita
"Effect of Oral Detergent on Blood Lipids"
Samuel Zelman, Topeka
"Home Care in the Treatment of Tuberculosis"
Charles F. Taylor, Norton
Chest x-ray film conference

6:00 p.m. Social hour

7:00 p.m. Dinner and election of officers
Guest speaker: Henry C. Sweany, Mt. Vernon, Missouri
"Histoplasmosis, Past and Present"

LOUISIANA CHAPTER

The annual meeting of the Louisiana Chapter will be held in Lecture Room A of the Touro Infirmary, New Orleans, on Sunday, May 3. Following is the program:

2:30 p.m. Panel discussion: Surgery in the Patient with Limited Pulmonary Reserve
"Preoperative Preparations"
John H. Seabury, New Orleans
"Anesthetic Management"
John Adriani, New Orleans
"Management of Surgery"
Lawrence H. Strug, New Orleans
"Postoperative Management"
Howard A. Buechner, New Orleans

PENNSYLVANIA CHAPTER

The first joint annual meeting of the Pennsylvania Chapter of the College and the Pennsylvania Trudeau Society will be held on April 16 at the Hotel Jermyn, Scranton. Following is the program:

9:45 a.m. David A. Cooper, Philadelphia, presiding
Consecutive Case Conference of Five Consecutive Cases Admitted to Barton Memorial Hospital, Philadelphia, and Five Consecutive Cases Admitted to Samuel G. Dixon State Hospital, South Mountain
Robert L. Mayock, Philadelphia, Moderator

12:00 noon Business meeting

2:00 p.m. Katharine R. Boucot, Philadelphia, presiding
"Benign Pneumoconiosis"
Oscar A. Sander, Milwaukee, Wisconsin
"Modern Concepts of Etiology and Management of Bronchial Asthma"
Leo H. Criep, Pittsburgh
Discussor: Sheldon G. Cohen, Wilkes-Barre
"Report on 1959 Veterans Administration, Army and Navy Therapy Conference"
Archibald Cohen, Butler, Pennsylvania
Discussor: William Weiss, Philadelphia
Symposium on Vascular Lesions of the Thoracic Aorta
Differential Diagnosis—Herbert Stauffer, Philadelphia
Surgical Management—Charles Kirby, Philadelphia
Discussion—William L. Jamison, Washington, D.C.
"Cooperative Study of Chemotherapy of Lung Cancer"
Henry P. Close, Philadelphia

OUR SILVER ANNIVERSARY MEETING

This is a very special year for the College and the intensive effort and thought which have gone into the preparation of the annual program must prove the intent of our dedicated program chairmen, Dr. Arthur M. Master and Dr. Coleman B. Rabin, to guarantee a brilliant and diversified scientific session. After perusing the program appearing on the following pages, members who have not completed plans to attend should certainly give further thought to making such arrangements.

In addition to a fascinating array of scientific papers, many thought-provoking panel discussions and symposiums, round table and fireside conference subjects, and an award-winning program of motion pictures, a tribute will be paid to the pioneers of the College on this memorable occasion.

The 25th Annual Meeting of the College will open on Wednesday, June 3rd, with the presentation of postgraduate seminars on heart and lung diseases. A particularly interesting Open Forum sponsored by the Council and Committee on Undergraduate Medical Education will be held in the afternoon, at which time the medical teaching programs in five medical schools will be presented and discussed. Other meetings that day concern the Executive Council and Board of Regents.

Thursday, June 4th, will be a most active administrative day with the scheduled annual meetings of the College councils and committees. At noon there will be a joint luncheon meeting of the Governors and Regents, to be followed by the Open Administrative Session where elections for the coming year will be held. Your president will report at this session the discussions held at a vitally important meeting held in Washington, D.C. by the Department of Health, Education, and Welfare last November. On Thursday afternoon there will also be Open Forums sponsored by the Council on Research and Council on Hospitals of the College.

The Silver Anniversary Convocation will be held on Thursday night, June 4th, when approximately 200 new Fellows will be awarded their certificates of Fellowship in the College. A very special Honorary Fellowship will be conferred and Dr. John F. Briggs, St. Paul, Minnesota, will deliver the Fourth Louis Mark Memorial Lecture. This will be the most impressive Convocation ceremony the College has ever had, with all participants gowned in academic robes and hoods. Your particular attention is called to the fact that the Convocation this year is being held on Thursday night, whereas at past meetings it has always taken place on Saturday preceding the cocktail party and Presidents' Banquet.

The scientific sessions will open on Friday morning, June 5th, and continue through Saturday and Sunday, June 6th and 7th. On Friday night the popular Fireside Conferences will be held, starting promptly at 8:15 p.m. Thirty-five subjects concerned with heart and lung diseases will be discussed. Besides these stimulating discussions, refreshments will be served to enhance the evening's entertainment.

Our annual cocktail party will be held on Saturday night, as usual, preceding the Presidents' Banquet. The fathers and sons of the College will be honored at the cocktail party. It is of extreme interest, and perhaps not properly credited, that a good number of Fellows of the College have a son, or even two sons, who are also members. This tribute, therefore, to these family groups is especially significant and appropriate at the time of our Silver Anniversary celebration. With the same feeling, a special tribute to the Charter Members of the College will be made at the time of the Presidents' Banquet. Of the 500 original Charter Members, there are more than 250 who are still active in the College.

For the ladies attending the Silver Anniversary Meeting there are two delightful luncheons planned, on Thursday and Friday, June 4th and 5th, as well as an inviting sightseeing tour which includes a visit to a champagne factory. Moreover, our ladies are an important part of the Convocation ceremony and the Banquet festivities, and we look forward to having them with us.

With such an excellent meeting in prospect, may I urge you to make arrangements to attend. Be sure to request hotel reservations at once. I sincerely hope to see you at the meeting.

Donald A. Mulley.

President

25th ANNUAL MEETING
AMERICAN COLLEGE OF CHEST PHYSICIANS
AMBASSADOR HOTEL, ATLANTIC CITY

POSTGRADUATE SEMINARS

Wednesday, June 3

Morning Sessions—9:00 a.m.

AM-1 PULMONARY DISEASE (MEDICAL)

Chairman:

J. J. Kirshner, Associate in Medicine, Jefferson Medical College, Philadelphia, Pennsylvania

9:00 A.M.—*The Importance of Physiologic Studies in the Diagnosis and Treatment of Pulmonary Disease*

Richard T. Catheart, Assistant Professor of Medicine, Jefferson Medical College, Philadelphia, Pennsylvania

9:45 A.M.—*Diagnostic Considerations and Procedures in Patients with Diffuse Pulmonary Disease*

Peter A. Theodos, Assistant Professor of Clinical Medicine, Jefferson Medical College, Philadelphia, Pennsylvania

10:30 A.M.—*Public Health Aspects of Chronic Pulmonary Disease—Problems of Control in a Large City*

Samuel C. Stein, Chief, Tuberculosis Control Section, Department of Public Health, City of Philadelphia, Pennsylvania

11:15 A.M.—*Current Status of Treatment of Pulmonary Tuberculosis*

Donald J. Ottenberg, Assistant Professor of Medicine, Temple University School of Medicine, Philadelphia, Pennsylvania

A ten-minute question and answer period will follow each lecture

AM-2 CARDIOLOGY (SURGICAL)

Chairman:

Julian Johnson, Professor of Surgery, University of Pennsylvania School of Medicine and Graduate School of Medicine, Philadelphia, Pennsylvania

9:00 A.M.—*The Present Status of Surgical Repair of Septal Defects in Children*

Robert E. Gross, William E. Ladd Professor of Child Surgery, Harvard Medical School; Head, Department of Surgery, Children's Hospital, Boston, Massachusetts

9:30 A.M.—*The Surgical Treatment of Aortic Stenosis*

Robert P. Glover, Assistant Professor of Clinical Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

10:10 A.M.—*The Surgical Treatment of Aortic Insufficiency*

Charles P. Bailey, Director, Bailey Thoracic Clinic; Former Professor and Head, Department of Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

10:55 A.M.—*The Surgical Repair of Mitral Insufficiency*

Henry T. Nichols, Acting Professor and Head, Department of Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

11:30 A.M.—*A Critical Evaluation of the Various Surgical Techniques in the Treatment of Coronary Artery Disease*

John L. Madden, Attending Surgeon and Director, Department of Surgery, St. Clare's Hospital, New York City

A ten-minute question and answer period will follow each lecture

Postgraduate Seminars (Continued)

Afternoon Sessions—2:00 p.m.

PM-1 PULMONARY DISEASE (SURGICAL)

Chairman:

Robert L. Mayock, Assistant Professor of Clinical Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

2:00 P.M.—Bronchoscopy in the Diagnosis and Treatment of Pulmonary Disease

Charles M. Norris, Clinical Professor of Laryngology and Bronchoesophagology, Chevalier Jackson Bronchoscopic Clinic, Temple University School of Medicine and Hospital, Philadelphia, Pennsylvania

2:40 P.M.—Surgical Treatment of Pulmonary Malignancy

Julian Johnson, Professor of Surgery, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

3:30 P.M.—Place of Surgery in the Treatment of Pulmonary Tuberculosis

George W. Willauer, Clinical Professor of Surgery, Jefferson Medical College, Philadelphia, Pennsylvania

4:00 P.M.—Problems in the Surgical Management of Patients with Respiratory Insufficiency

Thomas F. Nealon, Jr., Assistant Professor of Surgery, Jefferson Medical College, Philadelphia, Pennsylvania

A ten-minute question and answer period will follow each lecture

PM-2 CARDIOLOGY (MEDICAL)

Chairman:

William Likoff, Chief, Cardiovascular Section, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

2:00 P.M.—Recent Radiologic Advances in the Diagnosis of Heart Disease

J. Stauffer Lehman, Professor and Chairman, Department of Radiology, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

2:30 P.M.—The Fundamental Physiologic Abnormalities in Rheumatic Heart Disease

Harry Goldberg, Assistant Professor of Medicine, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

3:10 P.M.—Atypical Coronary Heart Disease

Nathaniel E. Reich, Clinical Assistant Professor of Medicine, State University of New York College of Medicine, Brooklyn, New York

3:55 P.M.—The Recognition and Treatment of Cardiac Arrhythmias Precipitated by Digitalis Toxicity

Samuel Bellet, Professor of Clinical Cardiology, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

4:30 P.M.—Price, Prejudice and Fact in Digitalis Therapy

John S. LaDue, Associate Professor of Medicine, Cornell University Medical College, New York City

A ten-minute question and answer period will follow each lecture

NOTE: These seminars on diseases of the chest will be presented at the Ambassador Hotel on Wednesday, June 3, and are open to all physicians. The registration fee for each seminar is $7.50.

Registration for the seminars must be made in advance and accompanied by the tuition fee; seating capacity is limited and reservations will be accepted in the order received. A coupon for this purpose will be found on page 470. Please indicate your preference by number.

It is also necessary to complete the reservation form on page 469

SCIENTIFIC PROGRAM

Friday, June 5

9:00 a.m.—Scientific Session No. 1

Chairmen:

Donald R. McKay, Buffalo, New York, President, American College of Chest Physicians

Seymour M. Farber, San Francisco, California, President-Elect, American College of Chest Physicians

CURRENT TRENDS IN CHEST MEDICINE—AN EVALUATION OF THE PRESENT STATUS AND THE DIRECTION IN WHICH WE ARE PROCEEDING

Introductory Remarks:

Coleman B. Rabin, New York City, Chairman, Pulmonary Section, Committee on Scientific Program

Physiological Research

Hurley L. Motley, Professor of Medicine and Director, Cardio-Respiratory Laboratory, University of Southern California School of Medicine, Los Angeles, California

Medical Treatment of Tuberculosis

Karl H. Pfuetze, Medical Director and Superintendent, Chicago State Tuberculosis Sanitarium, Chicago, Illinois

Cancericidal Drugs in Neoplastic Diseases of the Chest

Alfred Gellhorn, Associate Professor of Medicine and Director, Institute for Cancer Research, Columbia University College of Physicians and Surgeons, New York City

Radiotherapy in Thoracic Neoplasms

Ralph Phillips, Associate Attending Radiation Therapist, Memorial Center for Cancer and Allied Diseases, New York City

Air Pollution as it Affects Chest Conditions

Harry Heimann, Assistant Chief, Air Pollution Medical Branch, Division of Special Health Services, Public Health Service; Albert Roberts, Chief, Clinical Investigations, Air Pollution Medical Branch, Public Health Service; and Peter V. Hamill, Public Health Service, Washington, D.C.

Inhalation Therapy

Maurice S. Segal, Clinical Professor of Medicine, Tufts University School of Medicine, Boston, Massachusetts

9:00 a.m.—Scientific Session No. 2

Chairmen:

Donato G. Alcaron, Mexico City, Mexico

Edward A. Greco, Portland, Maine

Introductory Remarks:

Arthur M. Master, Chairman, Cardiovascular Section, Committee on Scientific Program

Prolonged By-pass of the Heart by Veno-Arterial Pump During Acute Stress Due to Myocardial Infarction and Pulmonary Embolism

James F. Dickson, Research Associate in Surgery; Neil A. J. Hamer, Assistant Director, Circulation Laboratory; James W. Dow, Director, Circulation Laboratory, Presbyterian Hospital, Philadelphia, Pennsylvania

Discussor: Robert P. Glover, Assistant Professor of Clinical Surgery, University of Pennsylvania Medical School, Philadelphia, Pennsylvania

Maintenance of Systemic Circulation in Cardiac Arrest by Mechanocardiac Pulsator

Norman J. Siderius, Resident, Department of Surgery; Gerald A. Jones, Assistant Resident, Department of Surgery; William E. Adams, Raymond Professor of Surgery; Peter V. Moulder, Associate Professor of Surgery, University of Chicago School of Medicine, Chicago, Illinois

Discussor: Arthur F. Reimann, Chief of Thoracic Surgery, Suburban Cook County Tuberculosis Sanitarium District, Hinsdale, Illinois

Assisted Circulation. Long Term Replacement of Lungs and/or Heart

Dwight E. Harken, Associate Professor of Clinical Surgery, Harvard Medical School, Boston, Massachusetts

Discussor: Thomas W. Mattingly, Director of Medical Education, Washington Hospital Center, Washington, D.C.

A Different Surgical Approach to the Problem of Mitral Stenosis

Charles P. Bailey, Director, Bailey Thoracic Clinic; William Likoff, Chief, Cardiovascular Section, Hahnemann Medical College and Hospital; Jacob Zimmerman, Resident Surgeon in Cardiovascular Surgery, Albert Einstein Medical Center, Philadelphia, Pennsylvania

Discussor: William Likoff, Chief, Cardiovascular Section, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

Friday, June 5 (Continued)

Surgical Correction of Persistent Atrio-Ventricular Canal (Ostium Primum). A Newly Rediscovered and Correctable Lesion
F. Henry Ellis, Head of a Surgical Section, Mayo Clinic, Rochester, Minnesota
Discussor: Charles Kirby, Assistant Professor of Surgery, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Open Heart Surgery for Tetralogy of Fallot
Robert E. Gross, Professor of Child Surgery, Harvard Medical School, Boston, Massachusetts
Discussor: Milton Weinberg, Instructor in Surgery, University of Illinois College of Medicine, Chicago, Illinois

Surgical Treatment of Ischemic Heart Disease
Robert P. Glover, Assistant Professor of Clinical Surgery, University of Pennsylvania Medical School, Philadelphia, Pennsylvania
Discussor: J. Roderick Kitchell, Associate Professor of Cardiology, University of Pennsylvania Graduate School of Medicine, Philadelphia, Pennsylvania

12:00 noon—*Round Table Luncheon Discussions* (See page 462)

2:00 p.m.—*Scientific Session No. 1*

Chairmen:
J. Winthrop Peabody, Sr., Washington, D.C.
Joseph C. Placak, Sr., Cleveland, Ohio

Panel on Treatment of Fungus Infections with Particular Reference to the Newer Therapeutic Agents

Moderator:
John H. Seabury, Professor of Medicine, Louisiana State University School of Medicine, New Orleans, Louisiana

Panel:
Michael L. Furcolow, Medical Director, Chief, Kansas City Field Station, Public Health Service, Kansas City, Kansas
M. L. Littman, Research Associate, Department of Microbiology, Mount Sinai Hospital, New York City
Wheelan D. Sutliff, Chief, Infectious Diseases Section, Veterans Administration Medical Teaching Group Hospital (Kennedy), Memphis, Tennessee
William A. Winn, Medical Director, Tulare-Kings Counties Hospital, Springville, California

3:00 p.m.—*Bronchitis and Asthma*

On the Relief of Bronchospasm and Induction of Alveolar Hyperventilation: A Comparative Study of Aerosol Medication Administered by Voluntary Hyperventilation and Intermittent Positive Pressure Breathing
Herman Froeb and Mabel Pearson, B.S., Scripps Clinic and Research Foundation, La Jolla, California

Causes of Death and Pathological Findings in Bronchial Asthma
James W. Messer, Department of Internal Medicine, Jackson Clinic and Foundation, Madison, Wisconsin; Gustavus A. Peters, Section of Medicine, Mayo Clinic and Mayo Foundation for Medical Education and Research, Rochester, Minnesota; Wallace A. Bennett, Thomas D. Dee Hospital, Ogden, Utah

3:40 p.m.—*Special Techniques in Roentgenology of the Chest*

Transverse Tomography of the Chest—A Third Dimension in Body-Section Radiography
Bernard Roswit, Chief, Radiotherapy Service, Veterans Administration Hospital; Sol M. Unger, Assistant Chief, Radiotherapy Service, Veterans Administration Hospital, Bronx, New York

Barium Sulfate as a Bronchographic Medium in Animal and Human Studies
Sidney W. Nelson, Professor of Radiology; William Molnar, Associate Professor of Radiology; Anthimos Christoforidis, Instructor in Radiology, Ohio State University College of Medicine, Columbus, Ohio

4:00 p.m.—*Clinical Studies in Pulmonary Diseases*

Hypertrophic Osteoarthropathy in Association with Metastatic Pulmonary Neoplasms
Arthur H. Aufses, Attending Thoracic Surgeon, Montefiore Hospital, New York City

Staphylococcal Pneumonitis in the Postoperative Patient
Edward H. Morgan, The Mason Clinic; Louis J. Lancaster, Resident in Medicine, Virginia Mason Hospital; G. Hugh Lawrence, The Mason Clinic; H. Rowland Pearsall, The Mason Clinic, Seattle, Washington

Friday, June 5 (Continued)

Mediastinal Tumors and Cysts in the Adult
Minas Joannides, Jr., Chief, Thoracic Surgical Section, Veterans Administration Center, Bay Pines, Florida; **Hiram T. Langston**, Clinical Associate Professor of Surgery, University of Illinois College of Medicine, Chicago, Illinois

A Closer Look at Pediatric Stridor
Joseph W. Peabody, Jr., Instructor in Thoracic Surgery; **Edgar W. Davis**, Professor of Thoracic Surgery, Georgetown University School of Medicine, Washington, D.C.

2:00 p.m.—*Scientific Session No. 2*

Chairmen:
B. Guy Begin, Montreal, Quebec, Canada
Miguel Canizares, Quezon City, Philippines

Incidence of Coronary Artery Disease in the Navajo Indian, Electrocardiographic and Autopsy Correlation
Richard B. Streeper, Chairman, Section of Cardiovascular Disease; **Robert U. Massey**, Chairman, Department of Medicine, Lovelace Clinic; **G. Liu**, Chief Medical Resident, Bataan Memorial Methodist Hospital; **C. H. Dillingham**, Member, Section of Metabolic and Endocrine Diseases, Lovelace Clinic; **A. Cushing**, Resident in Surgery, Veterans Administration Hospital, Albuquerque, New Mexico
Discussor: **Kurt Deuschele**, Assistant Professor, Department of Public Health and Preventive Medicine, Cornell University Medical College, New York City

Physiologic Evaluation of Angina Pectoris—Observations Before and After Revascularization Procedures
Norman Brachfeld, Gorlin Clinic; **Samuel A. Levine**, Clinical Professor of Medicine; **Richard Gorlin**, Associate in Medicine, Harvard Medical School, Boston, Massachusetts
Discussor: **Robert Case**, St. Luke's Hospital, New York City

Practical Clinical Applications of Direct Vectorcardiography
Stephen R. Elek, Associate Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles, California
Discussor: **Arthur Grishman**, Associate Attending Physician for Cardiology, Mt. Sinai Hospital, New York City

Application of Cine-Cardioangiography to the Study of Acquired Valvular and Degenerative Cardiovascular Lesions
F. Mason Sones, Jr., Director, Cardiac Catheterization Laboratory, Cleveland Clinic, Cleveland, Ohio
Discussor: **Israel Steinberg**, Assistant Clinical Professor of Medicine and Radiology, Cornell University Medical College, New York City

Clinical and Hemodynamic Features of Primary Myocardial Disease. Value of Myocardial Biopsies
Thomas W. Mattingly, Director of Medical Education, Washington Hospital Center, Washington, D.C.
Discussor: **William C. Manion**, Chief, Cardiovascular Surgery, Armed Forces Institute of Pathology, Washington, D.C.

Dissolution of Coronary Artery Thrombi by Plasmin
John S. LaDue, Associate Professor of Clinical Medicine, Cornell University Medical School, **Paul Ruegsegger**, Clinical Assistant Physician; **Irwin Nydick**, Clinical Assistant Physician, Memorial Hospital; **Ramon Abarquez**; **Eugene E. Cliffton**, Associate Professor of Clinical Surgery, Cornell University Medical School, New York City
Discussor: **David Adlersberg**, Associate Attending Physician, Metabolic Diseases, Mt. Sinai Hospital, New York City

Physiologic Rationale for the Use of Vasopressor Drugs in the Treatment of Cardiac Arrhythmias
Eliot Corday, Assistant Clinical Professor; **Herbert Gold**, Instructor in Medicine, University of California School of Medicine, Los Angeles, California; **John H. Williams**, Research Fellow, New England Center Hospital, Boston, Massachusetts
Discussor: **David Scherf**, Professor of Clinical Medicine, New York Medical College, New York City

Electrolytes and Water Metabolism in Heart Failure
Warren Braveman, Cardiorenal Laboratory, Second (Cornell) Medical Division, New York Hospital, New York City
Discussor: **Charles Goodrich**, Associate Director, Comprehensive Chair Program, Department of Medicine, New York Hospital, New York City

8:15 p.m.—Scientific Session

"Fireside Conferences"
Subjects and Discussion Leaders

Pulmonary Cavities

Howard A. Buechner, Chief, Medical Service, Veterans Administration Hospital, New Orleans, Louisiana

J. Maxwell Chamberlain, Assistant Clinical Professor of Surgery, Columbia University College of Physicians and Surgeons, New York City

Jose F. Valiente, Professor of Diseases of the Chest and Tuberculosis, Universidad de El Salvador, San Salvador, El Salvador

Problems in Endoscopic Photography

Chevalier L. Jackson, Professor of Laryngology and Bronchoesophagology, Temple University School of Medicine, Philadelphia, Pennsylvania

Kenneth C. Johnston, Assistant Clinical Professor of Bronchoesophagology, University of Illinois College of Medicine, Chicago, Illinois

Arthur M. Olsen, Professor of Medicine, Mayo Foundation, Graduate School of Medicine, University of Minnesota, Rochester, Minnesota

Indications and Contraindications of Cardiac Surgery in Acquired Congenital Heart Disease

Alvin A. Bakst, Director of Thoracic Surgery, Jewish Hospital of Brooklyn, Brooklyn, New York

Ivan D. Baronofsky, Chief of Surgery, Mt. Sinai Hospital, New York City

John Francis Dammann, Associate Professor of Surgical Cardiology, University of Virginia School of Medicine, Charlottesville, Virginia

Ephraim Donoso, Research Assistant in Cardiology, Mt. Sinai Hospital, New York City

Acquired Valvular Disease and Assisted Circulation

F. Henry Ellis, Head of a Surgical Section, Mayo Clinic, Rochester, Minnesota

Dwight E. Harken, Associate Professor of Clinical Surgery, Harvard Medical School, Boston, Massachusetts

Leslie A. Kuhn, Assistant Attending Physician for Cardiology, Mt. Sinai Hospital, New York City

The Pneumoconioses

Henry Dorfman, Senior Clinical Chest Physician, Mt. Sinai Hospital, New York City

J. Winthrop Peabody, Sr., Professor Emeritus, Diseases of the Respiratory System, Georgetown University School of Medicine, Washington, D.C.

Paul C. Swenson, Radiologist, Charles T. Miller Hospital, St. Paul, Minnesota

Two-Step Test

Thomas W. Mattingly, Director of Medical Education, Washington Hospital Center, Washington, D.C.

George Robb, Clinical Professor of Radiology, New York University College of Medicine, White Plains, New York

Isadore Rosenfeld, Instructor in Medicine, Cornell University Medical College, New York City

Chemotherapy of Tuberculosis

Robert V. Cohen, Associate Professor of Medicine, Temple University School of Medicine, Philadelphia, Pennsylvania

George G. Ornstein, Associate Professor of Medicine, New York Medical College, New York City

Maurice Small, Chief, Tuberculosis Service, Veterans Administration Hospital, East Orange, New Jersey

Management of Thoracic Emergencies

Gumersindo Blanco, Bailey Thoracic Clinic, Philadelphia, Pennsylvania

W. Ralph Deaton, Associate in Clinical Surgery, Bowman-Gray School of Medicine, Greensboro, North Carolina

Emil Naclerio, Chief Thoracic Surgeon, Harlem Hospital, New York City

Jaime F. Pou, Assistant Clinical Professor of Surgery, University of Puerto Rico School of Medicine, Hato Rey, Puerto Rico

Fireside Conferences (Continued)

Treatment of Heart Block: New Drugs and Electric Pacemaker (External and Internal)

Simon Dack, Associate Attending Physician in Cardiology, Mt. Sinai Hospital, New York City

Robert E. Gross, Professor of Child Surgery, Harvard Medical School, Boston, Massachusetts

Melvin Kahn, Mt. Sinai Hospital, New York City

The Solitary Nodule

William G. Cahan, Assistant Attending Surgeon, Memorial Center, New York City

Robert S. Cartwright, Head, Section of Thoracic and Cardiovascular Surgery, Lovelace Clinic and Foundation, Albuquerque, New Mexico

Paul S. Friedman, Radiologist, Rush Hospital, Philadelphia, Pennsylvania

John W. Vance, Millard Fillmore Hospital, Buffalo, New York

Value of Cardiac Catheterization in the Diagnosis of Acquired and Congenital Heart Disease

Norman Brachfeld, Gorlin Clinic, Boston, Massachusetts

Alvin Gordon, Associate Attending Physician, Mt. Sinai Hospital, New York City

William J. Kuzman, Assistant in Medicine, University of Southern California School of Medicine, La Jolla, California

Suppurative Diseases of the Lungs

Milton Gusack, Associate in Medicine, George Washington University School of Medicine, Washington, D.C.

James A. Kaufmann, Associate in Medicine, Emory University School of Medicine, Atlanta, Georgia

Henry J. Stanford, Consultant Thoracic Surgeon, Veterans Administration Hospital, Tucson, Arizona

Physiology of Pulmonary Heart Disease

William B. Jaques, Professor of Pathology, University of Oklahoma School of Medicine, Oklahoma City, Oklahoma

Irving Mack, Clinical Assistant Professor of Medicine, Chicago Medical School, Chicago, Illinois

William C. Manion, Chief, Cardiovascular Surgery, Armed Forces Institute of Pathology, Washington, D.C.

Atypical Tubercle Bacilli

Emil Bogen, Olive View Sanatorium, Olive View, California

William Lester, Chief of Staff, Suburban Cook County Tuberculosis Hospital-Sanitarium, Hinsdale, Illinois

Treatment of Cor Pulmonale

Mortimer Bader, Assistant Attending Physician, Mt. Sinai Hospital, New York City

Harry L. Jaffe, Assistant Attending Physician in Cardiology, Mt. Sinai Hospital, New York City

Abraham I. Schaffer, Department of Medicine, New York Medical College, New York City

Management of Coronary Heart Disease in Chronic Bronchitis and Emphysema

John F. Briggs, Associate Professor of Clinical Medicine, University of Minnesota Medical School, St. Paul, Minnesota

Nathaniel E. Reich, Clinical Assistant Professor of Medicine, State University of New York College of Medicine, Brooklyn, New York

John J. Sampson, Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

Surgery of Carcinoma of the Lung

Donald L. Paulson, Clinical Associate Professor of Thoracic Surgery, Southwestern Medical School of the University of Texas, Dallas, Texas

George P. Rosemond, Professor of Clinical Surgery, Temple University School of Medicine, Philadelphia, Pennsylvania

Irving A. Sarot, Attending Surgeon for Cardiac and Thoracic Surgery, Beth Israel Hospital, New York City

Fireside Conferences (Continued)

Newer Concepts in the Recognition and Treatment of Arrhythmias (Potassium, Versine, Vistaral, and Radioactive Iodine Treatment)

Samuel Bellet, Professor of Clinical Cardiology, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

Eliot Corday, Assistant Clinical Professor of Medicine, University of California School of Medicine, Los Angeles, California

Joseph H. Sage, Desert Hospital, Palm Springs, California

David Scherf, Professor of Clinical Medicine, New York Medical College, New York City

Pulmonary Function Testing

Ross C. Kory, Associate Professor of Medicine, Marquette University School of Medicine, Milwaukee, Wisconsin

Harold A. Lyons, Professor of Medicine, State University of New York, Brooklyn, New York

George A. Saxton, Associate Professor of Preventive Medicine, University of Illinois College of Medicine, Chicago, Illinois

Clinical Problems in Congestive Heart Failure

Warren Braveman, Cardiorenal Laboratory, Second (Cornell) Medical Division, New York Hospital, New York City

Richard P. Lasser, Assistant Attending Physician for Cardiology, Mt. Sinai Hospital, New York City

John H. Moyer, Professor and Head, Department of Medicine, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

Treatment of Pulmonary Insufficiency

Hylan A. Bickerman, Associate Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City

Israel Rappaport, Consulting Physician, Bellevue Hospital, New York City

E. E. Rockey, Clinical Instructor in Surgery, New York Medical College, New York City

Peter A. Theodos, Assistant Professor of Clinical Medicine, Jefferson Medical College, Philadelphia, Pennsylvania

Anticoagulant Drugs

William T. Foley, Assistant Professor of Clinical Medicine, Cornell University Medical College, New York City

John S. LaDue, Associate Professor of Clinical Medicine, Cornell University Medical College, New York City

Irving Wright, Professor of Clinical Medicine, Cornell University Medical College, New York City

Anesthesia in Thoracic Operations

Alfred Goldman, Chief of Thoracic Surgery, Cedars of Lebanon Hospital and City of Hope, Beverly Hills, California

Herbert C. Maier, Director of Surgery, Lenox Hill Hospital, New York City

Auscultation of the Heart: Advances in Phonocardiography and Its Clinical Applications

Selvin Bleifer, Mt. Sinai Hospital, New York City

Arthur Grishman, Assistant Attending Physician in Cardiology, Mt. Sinai Hospital, New York City

Joseph K. Perloff, Washington, D.C.

Diagnostic Techniques: Pleural and Prescalenous Biopsies; Exfoliative Cytology

Howard A. Andersen, Assistant Professor of Medicine, Mayo Foundation, Rochester, Minnesota

John B. Grow, Assistant Professor of Surgery, Colorado University Medical School, Denver, Colorado

G. Hugh Lawrence, Section of Surgery, Mason Clinic, Seattle, Washington

Mental Disturbances and Pulmonary Disease

Robert P. Barrell, Ph.D., Clinical Psychologist, Veterans Administration Hospital, Downey, Illinois

Otto L. Bettag, Director of Public Welfare, State of Illinois, Chicago, Illinois

P. J. Sparer, Professor of Psychiatry and Preventive Medicine, University of Tennessee College of Medicine, Memphis, Tennessee

Fireside Conferences (Continued)

Pulmonary Edema

Stephen R. Elek, Associate Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles, California

M. Jay Flipse, Jackson Memorial Hospital, Miami, Florida

Aldo A. Luisada, Associate Professor of Medicine and Director, Division of Cardiology, Chicago Medical School, Chicago, Illinois

Howard Moscovitz, Research Associate in Medicine, Mt. Sinai Hospital, New York City

Allergic Diseases

Ethan Allan Brown, Boston, Massachusetts

Morris Kaplan, Associate Professor of Medicine and Director, Allergy Research Unit, Chicago Medical School, Chicago, Illinois

Nontuberculous Bronchopulmonary Diseases in Children

Thomas G. Baffes, Assistant Attending Surgeon, Children's Memorial Hospital, Chicago, Illinois

Alberto Chattas, Professor of Pediatrics, National University of Cordoba School of Medicine, Cordoba, Argentina

Gordon E. Gibbs, Professor and Chairman, Department of Pediatrics, University of Nebraska College of Medicine, Omaha, Nebraska

Management of Tuberculosis

Paul K. Bornstein, Instructor in Medicine, New York Medical College, Asbury Park, New Jersey

Kurt Deuschele, Assistant Professor, Department of Public Health and Preventive Medicine, Cornell University Medical College, New York City

Miguel Jimenez, Clinical Professor of Chest Diseases, University of Mexico, Mexico City, Mexico

Leopoldo Molinari B., Medical Chief, Bronchopulmonary and Tuberculosis Department, Hospital Obrero de Lima, Lima, Peru

The Esophagus

Joseph P. Atkins, Clinical Professor of Bronchology and Esophagology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Henry J. Heimlich, Adjunct Thoracic Surgeon, Montefiore Hospital, New York City

The Lungs in Systemic Diseases

George L. Baum, Assistant Chief, Pulmonary Disease Section, Veterans Administration Hospital, Coral Gables, Florida

Eli Rubin, Professor of Clinical Medicine, Albert Einstein College of Medicine, Yeshiva University, New York City

Mauricio Teichholz, Assistant Professor of Endocrinology and Pathology, University of the Federal District, Rio de Janeiro, Brazil

Surgical Treatment of Tuberculosis

Miguel Canizares, Director, Quezon Institute, Quezon City, Philippines

Irving Shiner, Associate Clinical Professor of Thoracic Surgery, New York Medical College and Flower-Fifth Avenue Hospital, New York City

Carlos Zurita Gonzalez, Director, Comarcal Anti-tuberculosis Dispensary, Cabra de Cordoba, Spain

Emphysematous Blebs and Bullae

John W. Bell, Chief, Surgical Service, Veterans Administration Hospital, Seattle, Washington

William E. Neville, Clinical Instructor in Surgery, Western Reserve University School of Medicine, Cleveland, Ohio

Physiology of Emphysema

Howard G. Dayman, Assistant Professor of Medicine, University of Buffalo School of Medicine, Buffalo, New York

W. Y. Hallet, Associate in Medicine, University of Washington School of Medicine, Seattle, Washington

Angiocardiography in the Diagnosis of Cardiovascular Disease

Benjamin M. Gasul, Director of Pediatric Cardiology, Cook County Children's Hospital and Hektoen Institute for Medical Research, Chicago, Illinois

Sigmund Brahms, Associate Attending Radiologist, Mt. Sinai Hospital, New York City

Israel Steinberg, Assistant Clinical Professor of Medicine and Radiology, Cornell University Medical College, New York City

Saturday, June 6

9:00 a.m.—Scientific Session No. 1

Chairmen:

Dean B. Cole, Richmond, Virginia
Howell S. Randolph, Phoenix, Arizona

Panel on Air Transport of Patients with Respiratory Disease

Moderator:

Burgess L. Gordon, Director of Education, Coordinator of Research, and Consultant in Cardiopulmonary Physiology, Lovelace Foundation, Albuquerque, New Mexico

Panel:

W. P. Hannon, Director, Aircraft Engineering, American Airlines, Tulsa, Oklahoma
Lt. Colonel Robert B. Stonehill, MC, USAF, Chief, Pulmonary Disease Service and Pulmonary Physiology Laboratory, USAF Hospital, Lackland Air Force Base, Texas
Roger H. L. Wilson, Assistant Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

10:30 a.m.—Symposium on Bronchogenic Carcinoma

Unilateral Smoking Dog for Controlled Study of Effect of Cigarette Smoke on the Bronchial Mucosa
Samuel W. Hunter, Assistant Professor of Surgery, University of Minnesota; Dominic Bernardez, Surgical Service, St. Joseph's Hospital; Sister Victorine Long, Surgical Service, St. Joseph's Hospital, St. Paul, Minnesota

Serum Enzymes in Bronchogenic Carcinoma and Other Pulmonary Diseases
Lt. Jerome A. Gold, MC, USNR, Head, Chest Service, U.S. Naval Hospital, National Naval Medical Center, Bethesda, Maryland

Five-Year Survival After Surgery of Bronchogenic Carcinoma—An Analysis of 21 Cases
Donald B. Effler, Chief, Department of Thoracic Surgery; David Barr, Fellow, Department of Thoracic Surgery, Cleveland Clinic, Cleveland, Ohio

11:15 a.m.—Operations for Tracheal Reconstruction and Repair of Acquired Bronchoesophageal Fistula

Success and Failures in the Surgical Reconstruction of the Trachea and Bronchi in Children and Adults
Osler A. Abbott, Chief, Division of Thoracic Surgery, Grady Memorial Hospital and Emory University Hospital, Emory, Georgia

Experimental Repair of Tracheal Defects with Gallbladder Mucosa
John W. Bell, Chief of Surgery, Veterans Administration Hospital, Seattle, Washington

Treatment of Acquired, Non-malignant Esophagotracheal-Bronchial Fistula
Robert J. Jensik, Attending Thoracic Surgeon; Willard Van Hazel, Attending Thoracic Surgeon; Paul H. Holinger, Attending Bronchoesophagologist; Kenneth C. Johnston, Attending Bronchoesophagologist, Presbyterian-St. Luke's Hospital, Chicago, Illinois

9:00 a.m.—Scientific Session No. 2

Chairmen:

Arthur M. Master, Consultant Cardiologist, Mt. Sinai Hospital, New York City
Ephraim Donoso, Research Assistant in Cardiology, Mt. Sinai Hospital, New York City

Modern Graphic Devices, Roentgen Techniques and Recording Equipment in the Diagnosis and Surgery of Heart Disease

Machine and Physician in the Present and Future of Heart Disease
Arthur M. Master and **Ephraim Donoso**

Pathology of Surgically Correctable Cardiovascular Lesions
Lotte Strauss, Associate Pathologist for Pediatrics, Mt. Sinai Hospital, New York City

Auscultation and Phonocardiography. Clinical Applications
Arthur Grishman, Associate Attending Physician for Cardiology, Mt. Sinai Hospital, New York City

Saturday, June 6 (Continued)

Intracardiac Phonocardiography. Clinical Applications
Howard Moscovitz, Assistant Attending Physician for Medicine, Mt. Sinai Hospital, New York City

Clinical Value of the Vectorcardiogram, Pulse Tracings and Other Graphic Methods
Simon Dack, Associate Attending Physician for Cardiology, Mt. Sinai Hospital, New York City

Diagnostic Application of the Electrocardiogram
Richard P. Lasser, Assistant Attending Physician for Cardiology, Mt. Sinai Hospital, New York City

Modern Apparatus and Techniques in Right and Left Heart Catheterization
Alvin J. Gordon, Associate Attending Physician, Mt. Sinai Hospital, New York City

Newer Techniques in Localization of Shunts—Dye Dilution Curves, Gas Analysis, Radioactive Techniques
Leslie A. Kuhn, Assistant Attending Physician for Cardiology, Mt. Sinai Hospital, New York City

Advances in Radiographic Techniques
Sigmund A. Brahms, Associate Attending Radiologist, Mt. Sinai Hospital, New York City

Cardiac Monitoring During Surgery (Direct Pressure Recordings, etc.)
Gabriel Genkins, Clinical Assistant in Medicine, Mt. Sinai Hospital, New York City

12:00 noon—*Round Table Luncheon Discussions* ***(See page 463)***

2:00 p.m.—*Scientific Session No. 1*

Chairmen:
Alvis E. Greer, Houston, Texas
William A. Hudson, Detroit, Michigan

Symposium on Pulmonary Tuberculosis

FIFTH ANNUAL SELMAN WAKSMAN LECTURE
NEW JERSEY CHAPTER, AMERICAN COLLEGE OF CHEST PHYSICIANS

Is Pulmonary Disease, Often Fatal, Caused by Nonphotochromogenic ("Atypical") Acid-fast Mycobacteria, Communicable?
Horace E. Crow, Battey State Hospital, Rome, Georgia

BCG Vaccination of Student Nurses, a Ten Year Experience
Norman S. Blackman, John M. Shelley, Elizabeth K. Hoyt, Brooklyn Hospital, Brooklyn, New York

Treatment of Cavitary Pulmonary Tuberculosis with Cycloserine and Isoniazid Compared with Isoniazid-PAS
Patrick B. Storey, Director of Professional Services, Veterans Administration Hospital, Baltimore, Maryland

Circulating Antibodies in Active Tuberculosis and Other Granulomatous Diseases
Daniel L. Weiss, Pathologist and Director of Laboratories; Matthew Fusillo, Bacteriologist, District of Columbia General Hospital, Washington, D.C.

Saturday, June 6 (Continued)

3:15 p.m.—Symposium on Emphysema, Function Tests and Respiratory Aids

Clinical Observations in Patients with Pulmonary Insufficiency Treated by Permanent Tracheostomy
Edgar Mayer, Clinical Professor of Medicine, New York University-Bellevue Medical Center, School of Industrial Medicine, New York City

Studies in the Recognition and Treatment of Early Emphysema in Children
Roy F. Goddard, Director, Pediatric Research Department; Ulrich C. Luft, Head, Department of Physiology, Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico

Lung Volumes in Normal Tall Male Subjects
Norman G. Hepper, Section of Medicine; Ward S. Fowler, Section of Physiology, Mayo Clinic, Rochester, Minnesota

A Comparison of Various Segments of the Forced Expirogram with Maximum Breathing Capacity
William H. Anderson, Associate Chief of Medicine and Director, Cardiopulmonary Laboratory, Harlan Memorial Hospital, Harlan, Kentucky

Pulmonary Artery Pressure Studies: Does Over-distention of the Lung Cause Hypertension?
Arthur F. Reimann, Chief of Thoracic Surgery, Suburban Cook County Tuberculosis Sanitarium, Hinsdale; Edwin Tutt Long, Attending Surgeon, Department of Surgery; William E. Adams, Raymond Professor of Surgery, University of Chicago School of Medicine; Angelo Ozoa, Resident, Department of Surgery, Suburban Cook County Tuberculosis Sanitarium, Hinsdale, Illinois; Salvatore Nigro, Senior Assistant Resident, Department of Surgery, University of Chicago School of Medicine, Chicago, Illinois

Spirometric Patterns of Positive Pressure Breathing Therapy
Albert H. Andrews, Jr., Associate Clinical Professor of Bronchoesophagology, University of Illinois College of Medicine, Chicago, Illinois

Physiologic Effects of Combined Exercise and Intermittent Positive Pressure Breathing in Emphysema
Edwin R. Levine, Assistant Professor of Clinical Medicine, Chicago Medical School, Chicago, Illinois

Physiologic Auto-control of Mechanical Respirators
Sam E. Stephenson, Jr., Assistant Professor of Surgery; W. Young, Student Research Assistant; L. H. Montgomery, Consultant in Medical Electronics, Department of Anatomy; R. Batson, Associate Professor of Pediatrics, Vanderbilt University School of Medicine, Nashville, Tennessee.

2:00 p.m.—Scientific Session No. 2

Chairmen:

Ivan D. Baronofsky, New York City
Hugo W. Knipping, Cologne, Germany

Modern Graphic Devices, Roentgen Techniques and Recording Equipment in the Diagnosis and Surgery of Heart Disease

Anesthesia in Cardiac Surgery (Demonstration of Latest Machines and Recording Apparatus)
Elliott Jacobson, Assistant Attending Anesthesiologist, Mt. Sinai Hospital, New York City

Fundamentals of Open Heart Surgery (Pump Oxygenators, etc.)
Lawrence J. Zaroff, Mt. Sinai Hospital, New York City

Rationale of Surgical Conduct in Closed and Open Heart Procedures
Ivan D. Baronofsky, Clinical Professor of Surgery, Columbia University College of Physicians and Surgeons; Chief of Surgery, Mt. Sinai Hospital, New York City

Post-Operative Course in Cardiac Surgery: Management of Surgical Problems (Left Heart Distention, Hemorrhage, Tracheal, Bronchial, and Pulmonary Complications)
Isadore Kreel, Mt. Sinai Hospital, New York City

Post-Operative Course in Cardiac Surgery: Management of Medical Problems (Electrolyte and Fluid Balance, Arrhythmias, Over-Oxygenation, Infection and Left Heart Distention)
Leonard Steinfeld, Clinical Assistant in Pediatrics, Mt. Sinai Hospital, New York City

Discussion

Sunday, June 7

9:00 a.m.—Scientific Session No. 1

Chairmen:

Edward W. Hayes, Sr., Monrovia, California
Irving Willner, Newark, New Jersey

Atmospheric Influences on the Respiratory Tract

Use of a High Humidity Environment in the Treatment of Diseases of the Upper and Lower Respiratory Tract; Experiences in a Fog Room

Roe E. Wells, Jr., Associate in Medicine, Peter Bent Brigham Hospital, Boston, Massachusetts

Effects of Air Pollution and Humidity on Patients with Pulmonary Emphysema

Roger H. L. Wilson, Assistant Clinical Professor of Medicine; Nancy L. Wilson, Graduate Resident Dietitian; George J. L. Riba, Assistant Clinical Professor of Medicine; Seymour M. Farber, Associate Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

Atmospheric Electricity and Its Effect on the Respiratory System

Albert P. Krueger, Emeritus Professor of Bacteriology and Lecturer in Medicine, University of California School of Medicine; John C. Beckett, E.E., Chairman, Committee on Electrical Technology, Medicine and Biology, American Institute of Electrical Engineers; Richard F. Smith, Graduate Resident in Bacteriology, University of California School of Medicine, Berkeley, California

10:15 a.m.—Symposium on the Esophagus

Late Results of Treatment of Carcinoma of the Esophagus

David P. Boyd, Thoracic Surgeon, Lahey Clinic, Boston, Massachusetts

PANEL DISCUSSION ON ESOPHAGEAL MOTILITY STUDIES IN THE DIFFERENTIAL DIAGNOSIS OF SUBSTERNAL DISTRESS (covering achalasia, dyschalasia, diffuse esophageal spasm, hiatal hernia, scleroderma, differentiation between stricture, spasm and carcinoma)

Moderator:

Herman J. Moersch, Professor of Medicine, Mayo Foundation of University of Minnesota; Chairman, Section of Medicine, Mayo Clinic, Rochester, Minnesota

Panel:

William F. Blakemore, J. William White Assistant Professor of Surgical Research, Assistant Professor of Surgery, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Charles F. Code, Mayo Clinic, Rochester, Minnesota

J. P. Medelman, Clinical Associate Professor of Radiology, University of Minnesota Medical School, St. Paul, Minnesota

Max Som, Professor of Otolaryngology, New York University Postgraduate Medical School, New York City

9:00 a.m.—Scientific Session No. 2

Chairmen:

Carl C. Aven, Atlanta, Georgia
Miguel Jimenez, Mexico City, Mexico

Symposium on Primary Arterial Hypertension

Moderators:

Milton Mendlowitz, Associate Attending Physician, Mt. Sinai Hospital, New York City

Grace M. Roth, Professor of Physiology, Mayo Foundation, Rochester, Minnesota

I. DEFINITIONS, INCIDENCE AND NATURAL HISTORY

Kenneth G. Kohlstaedt, Professor of Medicine, Indiana University School of Medicine, Indianapolis, Indiana

Richard E. Lee, Assistant Professor of Medicine, Cornell University Medical College, New York City

Arthur M. Master, Consultant Cardiologist, Mt. Sinai Hospital, New York City

W. E. Miall, Member, Scientific Staff, Medical Research Council, Pneumoconiosis Research Unit, Cardiff, Wales

Discussion

Sunday, June 7 (Continued)

II. MECHANISMS

A. C. Corcoran, Staff, Cleveland Clinic, Cleveland, Ohio
J. Richard Crout, Clinical Associate Lecturer in Experimental Health Therapeutics, National Heart Institute, Bethesda, Maryland
Quentin B. Deming, Associate Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City
Milton Mendlowitz, Associate Attending Physician, Mt. Sinai Hospital, New York City

Discussion

III. TREATMENT

David S. Baldwin, Assistant Professor of Medicine, New York University College of Medicine, New York City
Harriet P. Dustan, Staff, Research Division, Cleveland Clinic Foundation, Cleveland, Ohio
Keith S. Grimson, Professor of Surgery, Duke University School of Medicine, Durham, North Carolina
John H. Moyer, Professor and Head, Department of Medicine, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

Discussion

12:00 noon—Round Table Luncheon Discussions *(See page 464)*

2:00 p.m.—Combined Scientific Session—Diseases Involving Heart and Lungs

Chairmen:
Henry C. Sweany, Mt. Vernon, Missouri
Arthur Q. Penta, Schenectady, New York

Panel on the Lungs in Heart Disease

Moderator:
John F. Briggs, Associate Professor of Clinical Medicine, University of Minnesota Medical School, St. Paul, Minnesota

Panel:
John Francis Dammann, Associate Professor of Surgical Cardiology, University of Virginia School of Medicine, Charlottesville, Virginia
Jesse E. Edwards, Consultant, Section of Pathologic Anatomy, Mayo Clinic; Professor of Pathology, Mayo Foundation, Graduate School, University of Minnesota, Rochester Minnesota
Benjamin Felson, Professor and Director, Department of Radiology, University of Cincinnati College of Medicine, Cincinnati, Ohio
William Likoff, Chief, Cardiovascular Section, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

3:00 p.m.—The Lungs and the Circulatory System

A Study of the Subgross Pulmonary Anatomy in Various Mammals
Richard F. McLaughlin, Lt., MC, USNR, Medical Service, Cardiopulmonary Laboratory, U. S. Naval Hospital, Oakland California; Walter S. Tyler, D.V.M., Assistant Professor of Anatomy, School of Veterinary Medicine, University of California; Robert O. Canada, Captain, MC, USN, Chief, Medical Service, U. S. Naval Hospital, Bethesda, Maryland

Relation of Inflation Pressure to Vascular Resistance in the Isolated Canine Lung
David E. Donald, Ph.D., Consultant in Surgical Research, Mayo Foundation, Rochester, Minnesota

Cardiopulmonary Studies in the Obese. Notes on the Pickwickian Syndrome
Josef R. Smith, Instructor in Medicine, University of Mississippi Medical Center, Jackson, Mississippi

4:00 p.m.—Panel on the Heart in Pulmonary Disease

Moderator:
George C. Griffith, Professor of Medicine and Coordinator of Cardiovascular Instruction, University of Southern California School of Medicine, Los Angeles, California

Panel:
Samuel Bellet, Professor of Clinical Cardiology, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania
David M. Spain, Associate Professor of Pathology, Columbia University College of Physicians and Surgeons; Director of Laboratory, Beth-El Hospital, Brooklyn, New York

ROUND TABLE LUNCHEONS

Friday, June 5

A-1 ***The Role of Trace Metals in Myocardial Function***

J. Roderick Kitchell, Associate Professor of Cardiology, University of Pennsylvania Graduate School of Medicine, Philadelphia, Pennsylvania

John H. Moyer, Professor and Head, Department of Medicine, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

Felix Wroblewski, Clinical Assistant in Medicine, State University of New York College of Medicine, Brooklyn, New York

Moderator: **George C. Griffith**, Professor of Medicine and Coordinator of Cardiovascular Instruction, University of Southern California School of Medicine, Los Angeles, California

A-2 ***Rheumatic Fever***

Alvin A. Bakst, Director of Thoracic Surgery, Jewish Hospital of Brooklyn, Brooklyn, New York

Alvan Feinstein, Assistant Medical Director, Irvington House, Irvington-on-Hudson, New York

Benjamin M. Gasul, Director of Pediatric Cardiology, Cook County Children's Hospital and Hektoen Institute for Medical Research, Chicago, Illinois

Nathaniel E. Reich, Clinical Assistant Professor of Medicine, State University of New York College of Medicine, Brooklyn, New York

Moderator: **Charles Goodrich**, Associate Director, Comprehensive Chair Program, Department of Medicine, New York Hospital, New York City

A-3 ***Minimal and Maximal of Pulmonary Function Determinations—Type of Test and the Equipment Required for Examinations in the Office, Hospital and Research Institutions***

Edward H. Bergofsky, Department of Medicine, Columbia University College of Physicians and Surgeons, New York City

Peter C. Luchsinger, Director, Cardio-Pulmonary Laboratory, Georgetown Medical Division, District of Columbia General Hospital, Washington, D.C.

Lt. Colonel Robert B. Stonehill, MC, USAF, Chief, Pulmonary Disease Service and Pulmonary Physiology Laboratory, USAF Hospital, Lackland Air Force Base, Texas

Moderator: **George R. Meneely**, Associate Professor of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee

A-4 ***Surgical Treatment of Carcinoma of the Lung***

Donato G. Alarcon, Professor of Clinical Medicine, University of Mexico, Mexico City, Mexico

Edgar W. Davis, Professor of Thoracic Surgery, Georgetown University School of Medicine, Washington, D.C.

Julian Johnson, Professor of Surgery, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Moderator: **Alton Ochsner**, Director of Surgery, Ochsner Clinic and Foundation Hospital, New Orleans, Louisiana

A-5 ***Anticoagulants in Diseases of the Heart and Lungs***

William Foley, Assistant Professor of Clinical Medicine, Cornell University Medical School, New York City

John S. LaDue, Associate Professor of Clinical Medicine, Cornell University Medical College, New York City

Harry L. Jaffe, Assistant Attending Physician in Cardiology, Mt. Sinai Hospital, New York City

Moderator: **Irving Wright**, Professor of Clinical Medicine, Cornell University Medical College, New York City

A-6 ***Tuberculosis in Children***

James B. Arey, Professor of Pathology, Temple University School of Medicine, Philadelphia, Pennsylvania

Edith Lincoln, Adjunct Professor of Pediatrics, New York University College of Medicine, New York City

Eugene T. McEnery, Clinical Professor of Pediatrics, Stritch School of Medicine, Loyola University, Chicago, Illinois

Moderator: **Jay Arthur Myers**, Professor (Emeritus) of Internal Medicine and Public Health, University of Minnesota Medical and Graduate Schools, Minneapolis, Minnesota

ROUND TABLE LUNCHEONS

Saturday, June 6

B-1 ***Serum Enzymes***

Irving Kroop, Associate in Cardiology and Pediatric Cardiology, Jewish Hospital, Brooklyn, New York

Felix Wroblewski, Clinical Assistant in Medicine, State University of New York College of Medicine, Brooklyn, New York

Moderator: **John J. Sampson**, Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

B-2 ***Medical vs. Surgical Treatment of Coronary Heart Disease***

Charles P. Bailey, Director, Bailey Thoracic Clinic, Philadelphia, Pennsylvania

M. Jay Flipse, Jackson Memorial Hospital, Miami, Florida

Harry Jaffe, Assistant Attending Physician in Cardiology, Mt. Sinai Hospital, New York City

Mark W. Wolcott, Associate Clinical Professor of Surgery, University of Miami School of Medicine, Coral Gables, Florida

Moderator: **John F. Briggs**, Associate Professor of Clinical Medicine, University of Minnesota Medical School, St. Paul, Minnesota

B-3 ***Inhalation Therapy***

Allan Hurst, Assistant Clinical Professor of Medicine, University of Colorado School of Medicine, Denver, Colorado

William F. Miller, Associate Professor of Medicine, University of Texas Southwestern Medical School, Dallas, Texas

Reginald H. Smart, Clinical Professor of Medicine and Coordinator of Chest Disease Instruction, University of Southern California School of Medicine, Los Angeles, California

Moderator: **Edwin R. Levine**, Assistant Professor of Clinical Medicine, Chicago Medical School, Chicago, Illinois

B-4 ***Surgery of the Esophagus***

John Garlock, Consulting Surgeon, Mt. Sinai Hospital, New York City

John H. Harter, Assistant Professor of Surgery, University of Louisville School of Medicine, Louisville, Kentucky

Elmer C. Rigby, Surgeon, Cedars of Lebanon Hospital, Los Angeles, California

Moderator: **David H. Waterman**, Senior Attending Thoracic Surgeon, University of Tennessee Memorial Research Center and Hospital, Knoxville, Tennessee

B-5 ***Use and Dangers of Steroids in Diseases of the Lungs and Heart***

Sidney Blumenthal, Attending Pediatric Cardiologist, Mt. Sinai Hospital, New York City

Harry Shubin, Chief, Pulmonary Diseases, Philadelphia General Hospital, Philadelphia, Pennsylvania

Leon Unger, Associate Professor of Medicine, Northwestern University Medical School, Chicago, Illinois

Moderator: **David B. Radner**, Director, Chest Department, Michael Reese Hospital, Chicago, Illinois

B-6 ***Extrapulmonary Tuberculosis***

David Bosworth, Professor and Director of Orthopedic Surgery, New York Polyclinic Medical School and Hospital, New York City

Monroe Greenberger, New York City

Irving J. Selikoff, Associate Attending Physician for Thoracic Diseases, Mt. Sinai Hospital, New York City

Moderator: **Milton I. Levine**, Associate Professor of Clinical Pediatrics, New York Hospital-Cornell Medical Center, New York City

ROUND TABLE LUNCHEONS

Sunday, June 7

C-1 ***Pulmonary Hypertension***

Sidney Blumenthal, Attending Pediatric Cardiologist, Mt. Sinai Hospital, New York City

Clarence Crafoord, Professor and Head, Department of Thoracic Surgery, Karolinska Sjukhuset, Stockholm, Sweden

Arthur Grishman, Assistant Attending Physician in Cardiology, Mt. Sinai Hospital, New York City

Israel Steinberg, Assistant Clinical Professor of Medicine and Radiology, Cornell University Medical College, New York City

Moderator: **Jesse E. Edwards**, Consultant, Section of Pathological Anatomy, Mayo Clinic; Professor of Pathology, Mayo Foundation, Graduate School University of Minnesota, Rochester, Minnesota

C-2 ***Diet, Atherosclerosis and Coronary Artery Disease***

David Adlersberg, Associate Attending Physician, Metabolic Diseases, Mt. Sinai Hospital, New York City

Herbert Pollack, Assistant in Medicine, Columbia University College of Physicians and Surgeons, New York City

Isadore Rosenfeld, Instructor in Medicine, Cornell University Medical College, New York City

Moderator: **Robert E. Olson**, Professor and Head, Department of Biochemistry and Nutrition, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

C-3 ***Emphysema***

Milton V. Davis, Clinical Instructor in Surgery, University of Texas Southwestern Medical School, Dallas, Texas

Alfred S. Dooneief, Attending Physician, Montefiore Hospital, New York City

Joseph F. Tomashefski, Assistant Professor of Medicine and Physiology, Ohio State University College of Medicine, Columbus, Ohio

Moderator: **Andrew L. Banyai**, Clinical Professor of Medicine Emeritus, Marquette University School of Medicine (Milwaukee, Wisconsin), Chicago, Illinois

C-4 ***Detection of Early Carcinoma***

Katharine R. Boucot, Professor of Preventive Medicine, Woman's Medical College of Pennsylvania, Philadelphia, Pennsylvania

Oscar H. Friedman, Associate Physician for Chest Diseases, Mt. Sinai Hospital, New York City

Seymour Fiske Ochsner, Radiologist, Ochsner Clinic, New Orleans, Louisiana

Moderator: **Seymour M. Farber**, Chief, University of California Tuberculosis and Chest Service, San Francisco General Hospital, San Francisco, California

C-5 ***Antibiotic Treatment of Chronic Nonspecific Pulmonary Infections and Bacterial Endocarditis***

Gustav J. Beck, Instructor in Medicine, Columbia University College of Physicians and Surgeons, New York City

Benson Bloom, Veterans Administration Hospital, Bronx, New York

Robert Case, Attending Physician, St. Luke's Hospital, New York City

Moderator: **Alfred Goldman**, Associate Professor of Clinical Medicine and Director, Medical Chest Service, Washington University School of Medicine, St. Louis, Missouri

C-6 ***Management of Failures in the Medical Treatment of Tuberculosis—Retreatment and Surgery***

Sumner Cohen, Assistant Medical Director, Glen Lake Sanatorium, Oak Terrace, Minnesota

Sidney Dressler, Medical Director, National Jewish Hospital, Denver, Colorado

Lt. Colonel David E. Thomas, MC, USA, Chief, Thoracic Surgical Service, Valley Forge Army Hospital, Phoenixville, Pennsylvania

Moderator: **Colonel James A. Wier**, MC, USA, Chief, Pulmonary Disease Service, Fitzsimons Army Hospital, Denver, Colorado

SPECIAL EVENTS

Wednesday, June 3

3:30 p.m.—OPEN FORUM SPONSORED BY THE COUNCIL AND COMMITTEE ON UNDERGRADUATE MEDICAL EDUCATION

Undergraduate Teaching of Chest Diseases

The Council and Committee on Undergraduate Medical Education have selected the teaching programs in five medical schools, as they relate to diseases of the chest, which will be presented by members of the College affiliated with those schools. The discussion of audiovisual aids in such teaching will be presented. This will include the use of tape recordings and large-screen television demonstrations of clinical and laboratory experimental material.

Moderator: **William M. Lees,** Clinical Associate Professor of Surgery, Stritch School of Medicine, Loyola University, Chicago, Illinois

Panel: **Winthrop N. Davey,** Associate Professor of Internal Medicine, University of Michigan School of Medicine, Ann Arbor, Michigan

Stephen R. Elek, Associate Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles, California

James Feffer, Jr., Assistant Clinical Professor of Medicine, George Washington University School of Medicine, Washington, D.C.

Daniel E. Jenkins, Professor of Medicine, Baylor University College of Medicine, Houston, Texas

Questions and discussion from the floor.

Thursday, June 4

4:00 p.m.—OPEN FORUM SPONSORED BY THE COUNCIL ON HOSPITALS

Home Treatment Versus Sanatorium Treatment of Tuberculosis

In view of its importance, the Council on Hospitals has invited a group of competent physicians to discuss this problem. Members of the College who are interested in this subject are invited to submit questions to the chairman in advance of the meeting. Please send questions to American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Chairman: **Otto L. Bettag,** Director, Illinois Department of Public Welfare, Chicago, Illinois

Panel: **Leonard C. Evander,** Director, Mount View Hospital, Lockport, New York

Jerome R. Head, Assistant Professor of Surgery, Northwestern University Medical School Chicago, Illinois

Hollis E. Johnson, Professor of Clinical Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee

Arthur B. Robins, Director, Bureau of Tuberculosis, New York City Department of Health, New York

Questions and discussion from the floor.

Thursday, June 4

4:00 p.m.—OPEN FORUM, COUNCIL ON RESEARCH

Alvan L. Barach, New York City, Chairman, Council on Research, presiding

Presentation of Committee Reports

Committee on Physiologic Therapy
Albert H. Andrews, Chicago, Illinois, Chairman

Committee on Pulmonary Diseases in Children
Roy F. Goddard, Albuquerque, New Mexico, Chairman

Committee on Pulmonary Surgery
Alfred Goldman, Beverly Hills, California, Chairman

Committee on Non-Surgical and Drug Therapy
Alexander Libow, Miami Beach, Florida, Chairman

Committee on Cardiovascular Disease
Arthur M. Master, New York City, Chairman

Committee on Bronchoesophagology
Arthur M. Olsen, Rochester, Minnesota, Chairman

Committee on Allergy
Leon Unger, Chicago, Illinois, Chairman

Committee on Chemotherapy and Antibiotics
James A. Wier, Denver, Colorado, Chairman

Questions and discussion from the floor.

ADMINISTRATIVE SESSIONS

Wednesday, June 3

10:00 a.m.—Executive Council

2:00 p.m.—Board of Regents

4:30 p.m.—Committee on Nominations

Thursday, June 4

9:00 a.m.—Meetings of all Councils and Committees

9:00 a.m.—Examinations for Fellowship (written)

12:00 noon—LUNCHEON, JOINT MEETING

Board of Governors and Board of Regents

Howell S. Randolph, Phoenix, Arizona, Chairman, Board of Governors, presiding

Awarding of Certificates of Merit to Past-Presidents of College Chapters

Donald R. McKay, Buffalo, New York, President

Presentation of Reports

Reports of Chairmen, Sections on Cardiovascular Disease

Committee on Undergraduate Medical Education
William M. Lees, Chicago, Illinois, Chairman

Council on Postgraduate Medical Education
J. Winthrop Peabody, Sr., Washington, D.C., Chairman

Council on Research
Alvan L. Barach, New York City, Chairman

Council on Hospitals
Otto L. Bettag, Chicago, Illinois, Chairman

Committee on Membership
Chevalier L. Jackson, Philadelphia, Pennsylvania, Chairman

Committee on College Essay Contest
H. Allan Novack, Boston, Massachusetts, Chairman

College Books
Burgess L. Gordon, Albuquerque, New Mexico

Committee on Non-Surgical and Drug Therapy
Alexander Libow, Miami Beach, Florida, Chairman

Council on International Affairs
Andrew L. Banyai, Chicago, Illinois, Chairman

Silver Anniversary, Homecoming Meeting
Roy F. Goddard, Albuquerque, New Mexico

Silver Anniversary, Interim Session
Alvis E. Greer, Houston, Texas

1:30 p.m.—Meeting, Oral Examiners

2:00 p.m.—Examinations for Fellowship (oral)

2:00 p.m.—OPEN ADMINISTRATIVE SESSION

Donald R. McKay, Buffalo, New York, President, presiding

Report of the Historian
Carl C. Aven, Atlanta, Georgia

Report of the Treasurer
Charles K. Petter, Waukegan, Illinois

Report of the Executive Director
Murray Kornfeld, Chicago, Illinois

Report of the Committee on Nominations
James H. Stygall, Indianapolis, Indiana

Election of Officers

Report of the Meeting with the Department of Health, Education, and Welfare, Washington, D.C., November 1958
Donald R. McKay, Buffalo, New York, President

3:00 p.m.—Joint Meeting, Members of the National and State Committees on Membership, College Chapter Officials, and members of the Committee on Liaison with State and County Medical Societies

Chevalier L. Jackson, Philadelphia, Pennsylvania, Chairman, Committee on Membership, presiding

Panel Discussion on Membership Problems and Chapter Activities

Administrative Sessions (continued)

8:30 p.m.—**ANNUAL CONVOCATION**
Donald R. McKay, Buffalo, New York, President, presiding

FOURTH ANNUAL LOUIS MARK LECTURE
Optimism in Heart Disease
John F. Briggs, Associate Professor of Clinical Medicine, University of Minnesota Medical School, Minneapolis, Minnesota

Conferring of Honorary Fellowships and Fellowships

Address
Seymour M. Farber, San Francisco, California, President-Elect, American College of Chest Physicians

Participants in the Convocation ceremonies will be required to wear academic robes.

Friday, June 5

2:00 p.m.—Committee on Insurance
3:00 p.m.—Editorial Board
5:00 p.m.—Chapter Meetings
5:00 p.m.—Board of Examiners
5:00 p.m.—**COMMITTEE ON TUBERCULOSIS**
Lewis S. Jordan, Granite Falls, Minnesota, Chairman, presiding
Guest Speaker: **J. Arthur Myers**, Professor of Medicine and Public Health (Emeritus), University of Minnesota Medical and Graduate Schools, Minneapolis, Minnesota
Subject: ***What Needs to be Accomplished to Eradicate Tuberculosis?***

Saturday, June 6

9:00 a.m.—Executive Council
7:00 p.m.—Cocktail Party
7:30 p.m.—**ANNUAL PRESIDENTS' BANQUET**
An evening for fun—no speeches
9:30 p.m.—After-Dinner Dancing

Sunday, June 7

8:00 a.m.—Past-Presidents' Breakfast
10:00 a.m.—Executive Council
2:30 p.m.—Board of Regents

LADIES ACTIVITIES

Ladies attending the meeting are invited to register and receive guest badges. Tickets for the ladies luncheons and sightseeing tour are limited and should be ordered in advance, if possible. Remaining tickets may be purchased at the Ladies Registration Desk on Wednesday, June 3 or on Thursday morning, June 4.

Thursday, June 4

1:00 p.m.—Luncheon, Sheraton Ritz-Carlton Hotel
Dramatic presentations from plays by Eugene O'Neill will be presented by Mrs. John E. Devine
8:30 p.m.—College Convocation, Ambassador Hotel

Friday, June 5

10:45 a.m.—Sightseeing Tour and Visit to a Champagne Factory
1:00 p.m.—Luncheon, Linwood Country Club
Musical selections will be presented by Mr. Pedro Albani

Saturday, June 6

7:00 p.m.—College Cocktail Party, Ambassador Hotel
7:30 p.m.—Annual Presidents' Banquet, Ambassador Hotel
9:30 p.m.—After-Dinner Dance

Ladies Reception Committee

Honorary Chairmen

Mrs. Donald R. McKay Mrs. Murray Kornfeld Mrs. Irving Willner

Mrs. Charles Hyman, *Chairman*

Mrs. Lewis Baum
Mrs. S. Eugene Dalton
Mrs. Max Gross
Mrs. Allan Rieck
Mrs. Edward B. Tyson
Mrs. Clarence B. Whims

Mrs. Lawrence A. Wilson

MOTION PICTURE PROGRAM

The following is a tentative program of films dealing with diseases of the chest which will be shown concurrently with the scientific program on Friday, Saturday and Sunday, June 5, 6 and 7. Additional films are being considered by the Committee on Motion Pictures for presentation.

Surgical Reconstruction of the Cervical Trachea
Osler A. Abbott, Emory University School of Medicine, Atlanta, Georgia

Bronchocinematography
Shogo Awataguchi, The Research Institute for Tuberculosis and Leprosy, Tohoku University, Sendai, Japan

Ventricular Aneurysm Following Myocardial Infarction: Surgical Excision Using Cardiopulmonary Bypass
Denton A. Cooley, Baylor University College of Medicine, Houston, Texas

Correction of an Ostium Primum Type of Atrioseptal Defect Utilizing Extracorporeal Bypass
Philip Crastnopol and Alvin Bakst, Jewish Chronic Disease Hospital, Brooklyn, New York

Tumors of the Trachea and Bronchi
Paul H. Holinger and Kenneth C. Johnston, Chicago, Illinois

Forgut Cyst of the Esophagus
George A. Higgins, Veterans Administration Hospital, Kansas City, Missouri

Direct Vision Correction of Mitral Insufficiency Utilizing the Heart-Lung Machine
C. Walton Lillehei and Richard L. Varco, University of Minnesota Medical School and Variety Club Hospital, Minneapolis, Minnesota

Resectional Procedures in Pulmonary Tuberculosis
Ralph B. Lynn, University of Saskatchewan and Anti-Tuberculosis League of Saskatchewan, Saskatoon, Saskatchewan, Canada

Surgical Repair of Atrial Septal Defect Utilizing the Atrial Well Technique
JD Mortensen, Latter-Day Saints Hospital, Salt Lake City, Utah

Closure of Interauricular Septal Defect Under Hypothermia
Eric M. Nanson, University of Saskatchewan, Saskatoon, Saskatchewan, Canada

The Treatment of Coronary Arterial Heart Disease by Internal Mammary Artery Implantation
Arthur Vineberg, Montreal, Quebec, Canada

TECHNICAL EXHIBITORS

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Chicago, Illinois

Mine Safety Appliance Company
Pittsburgh, Pennsylvania

Mist O_2 Gen Equipment Company
Oakland, California

J. J. Monaghan Company
Denver, Colorado

National Medical Pumps & Specialties
Boonton, New Jersey

OEM Corporation
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Sherman Laboratories
Detroit, Michigan

Thompson Engineering Products
Boulder, Colorado

Winthrop Laboratories
New York City

ADVANCE REGISTRATION

There is no registration fee for members

The registration fee for non-members is $25.00

By completing this form and returning it at once to the Executive Offices of the College, you will avoid having to stand in line at the Registration Desk of the annual meeting in Atlantic City. Your badge and program, as well as luncheon, banquet and seminar tickets, will be prepared in advance and will be awaiting your arrival at the Ambassador Hotel. Please complete both sides of the Advance Registration Form and mail promptly. Thank you.

Non-members must enclose a registration fee of $25.00 with this form. Please make checks payable to **American College of Chest Physicians.**

Return the form to: American College of Chest Physicians
112 East Chestnut Street
Chicago 11, Illinois

FOR HOTEL RESERVATIONS, WRITE DIRECTLY TO THE AMBASSADOR HOTEL, ATLANTIC CITY

Advance Registration Form

.....Member .....Non-member

Please Print

Name .....

Address .....

City and State .....

Accompanied by .....

Hotel.....Arrival date.....Departure.....

Reservation Form—Annual Presidents' Banquet

Saturday, June 6, 1959 Cocktails-Dinner-Dancing
Ambassador Hotel, Atlantic City **Tickets: $9.75 each**

I wish to reserve.....tickets for the Annual Presidents' Banquet, Saturday, June 6, 7:00 p.m. (price includes cocktails, dinner and dancing).

ALL SEATS RESERVED

RESERVATION FORM

Annual Presidents' Banquet

All places at the Annual Presidents' Banquet are reserved. Tables will be assigned in order requests are received. Please order your tickets at once so that you may be assigned your table early. Tables for ten may be reserved upon receipt of payment for tickets and names of persons in the party. Special plans are being made for this Silver Anniversary Banquet and you will not want to miss it! A banquet reservation form may be found on the reverse side of this page.

Postgraduate Seminars

The program of postgraduate seminars appears on pages 448-449 of this issue of the journal. There is a tuition fee of $7.50 for each seminar. Registration for the postgraduate seminars is limited and reservations will be accepted in the order received. Please use the reservation form on this page and submit promptly to the executive offices of the College.

Round Table Luncheons

Round table luncheon discussions will be held on Friday, Saturday and Sunday, June 5, 6 and 7. The program of subjects may be found on pages 462-463-464 of this journal. As tickets for the round table discussions are usually sold out in advance of the meeting, members are urged to make their reservations at once. Please submit the reservation form at the bottom of this page.

Postgraduate Seminars, Wednesday, June 3

$7.50 each for members
Included in $25.00 registration fee for non-members

Morning Sessions (9 a.m.-12 noon)		**Afternoon Sessions (2:00-5:00 p.m.)**	
First choice	A.M.....	First choice	P.M.....
Second choice	A.M.....	Second choice	P.M.....

Please indicate choice by number as listed in program.

Round Table Luncheons

Tickets: $4.00 each

	Friday, June 5	**Saturday, June 6**	**Sunday, June 7**
First choice	A-.....	B-.....	C-.....
Second choice	A-.....	B-.....	C-.....
Third choice	A-.....	B-.....	C-.....

Please indicate choice by number as listed in program.

I am enclosing my check in the amount of $.....for reservations as indicated on this form.

Please make checks payable to **American College of Chest Physicians.**

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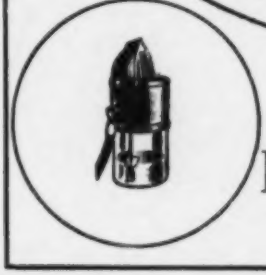
Preoperative Recognition and Treatment of Bronchopulmonary Disease: William F. Miller, MD; J. Robert Cade, MD, and Ivan E. Cushing, MD. Anesthesiology, Vol. 18, No. 3, pp. 483-497, May-June, 1957.

Considerations in Humidification by Nebulization: Ivan Cushing, MD, and William F. Miller, MD. Diseases of the Chest, Oct. 1958, Vol. XXXIV, No. 4.

An Aerosol Method of Producing Bronchial Secretions in Human Subjects: A Clinical Technique for the Detection of Lung Cancer. Hylan Bickerman, MD, FCCP; Edith Sproul, MD, and Alvan L. Barach, MD, FCCP. Diseases of the Chest, April, 1958, Vol. XXXIII, No. 4.

UNDERWRITERS LABORATORIES APPROVED



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